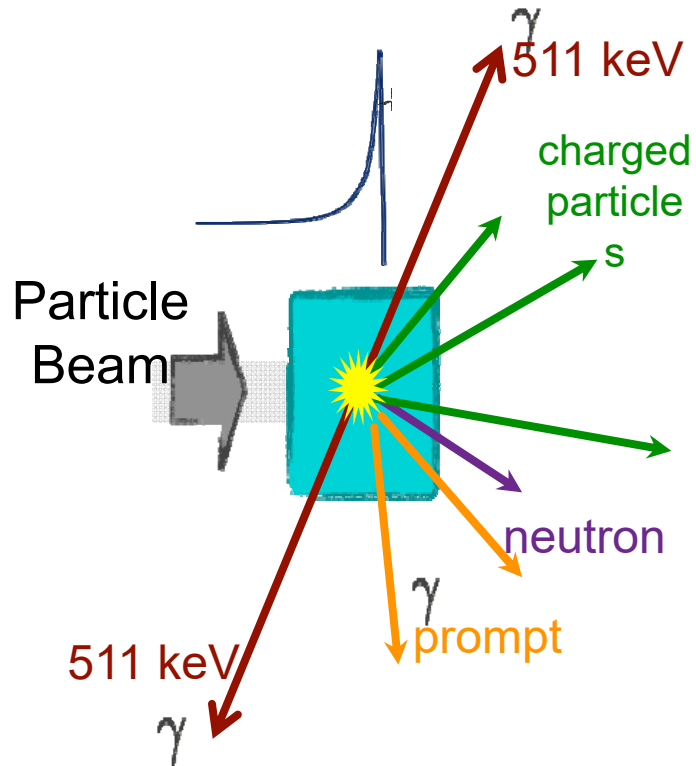


Proton therapy monitoring using PET

Proton as a projectile



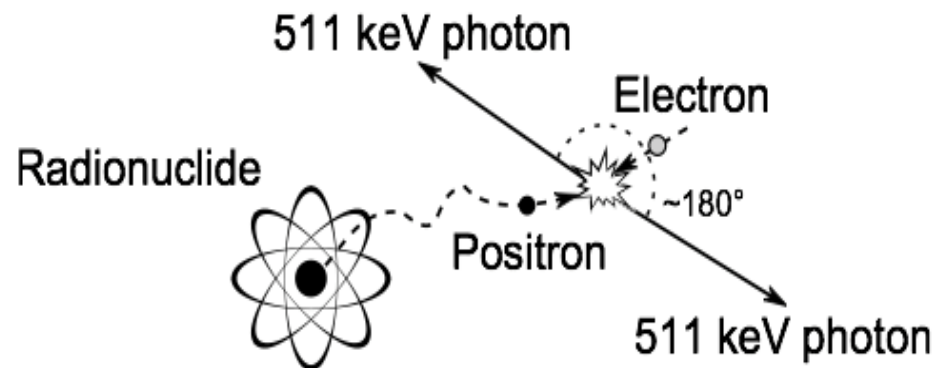
Fragmentation of the target:



$$\tau_{^{15}\text{O}} = 121.8 \text{ s}$$

$$\tau_{^{11}\text{C}} = 1222.8 \text{ s}$$

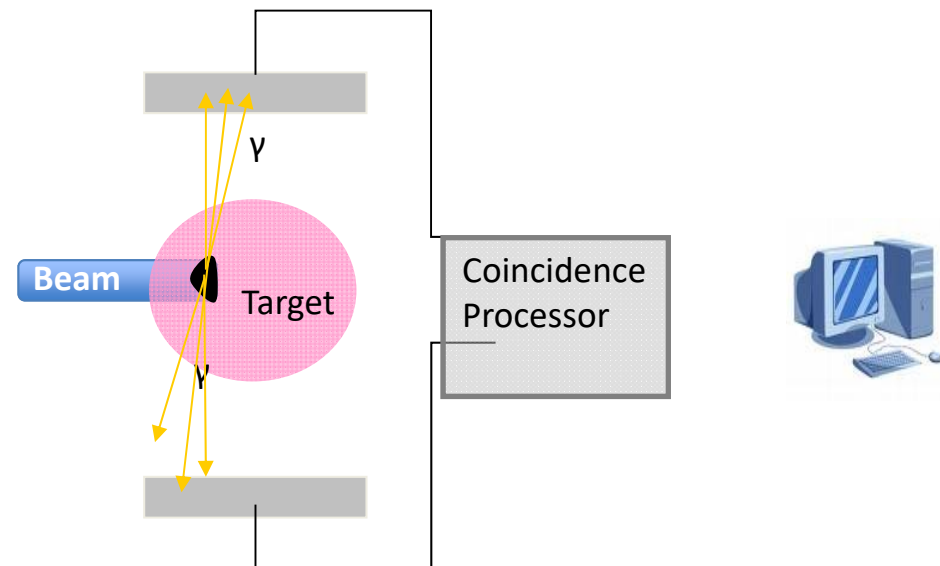
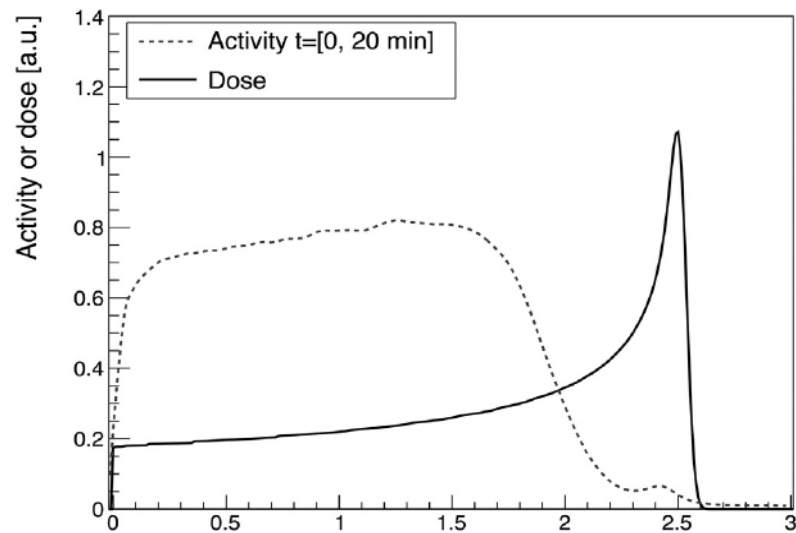
[15-20 MeV threshold for p-induced nuclear reactions]



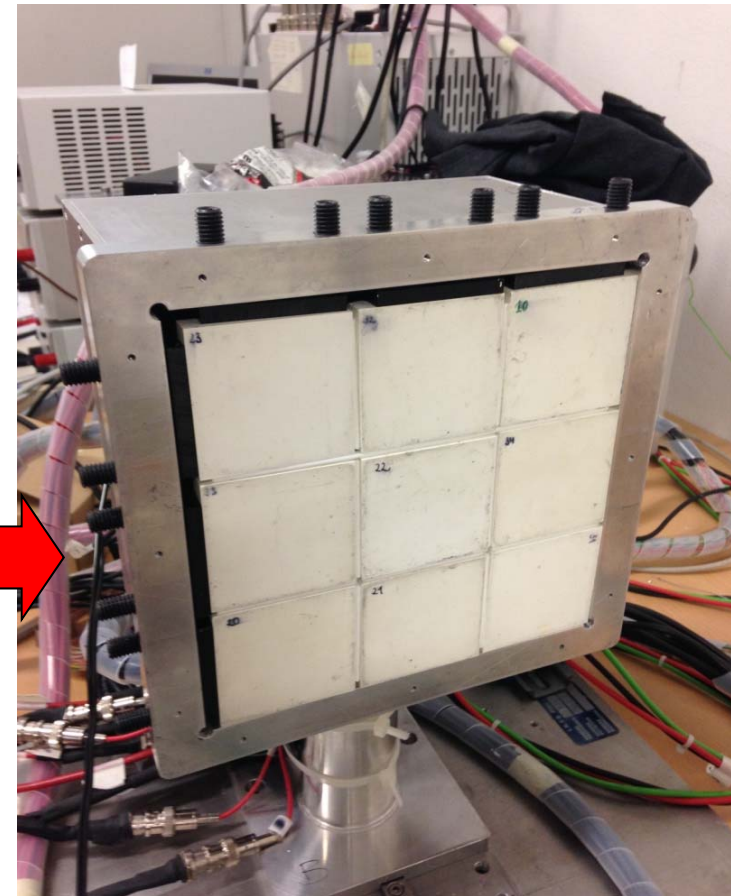
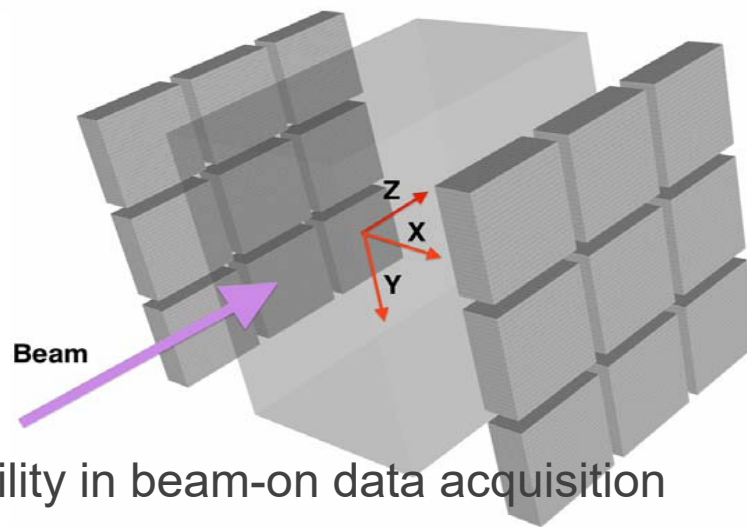
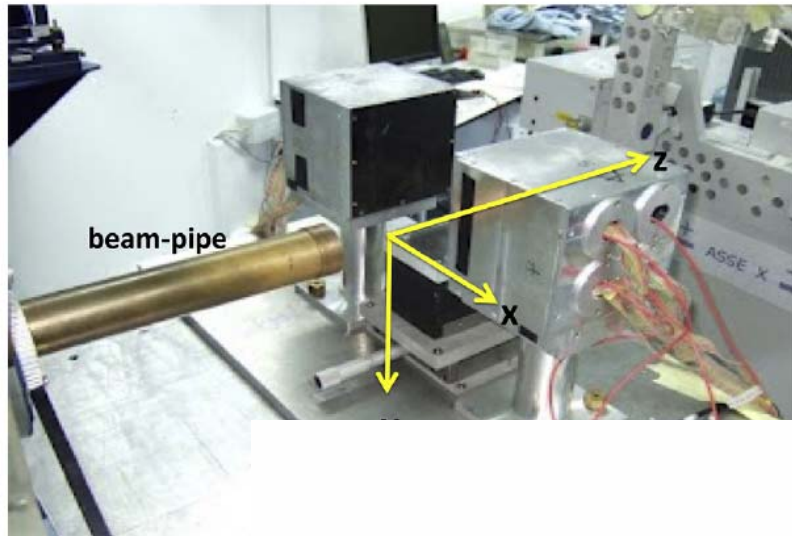
Measuring the β^+ activated volume we monitor the treatment

Dose and activity

- Most consolidated way to verify the delivered dose is by means of PET
- Hadron beams induce β^+ activity in patient
- Relation between activity and dose is indirect

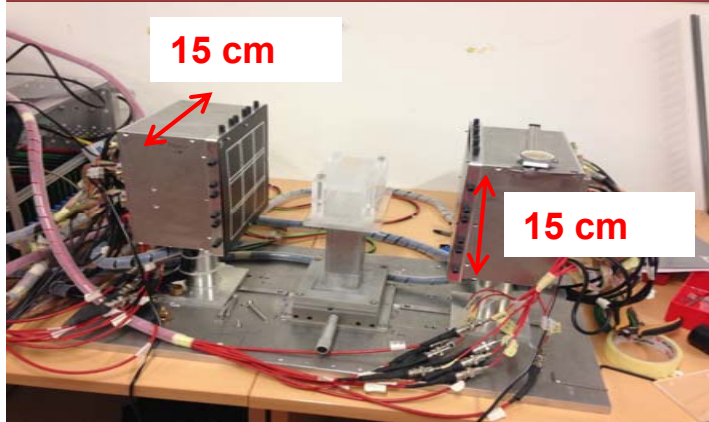


From the 4vs4 to 9vs9 prototype

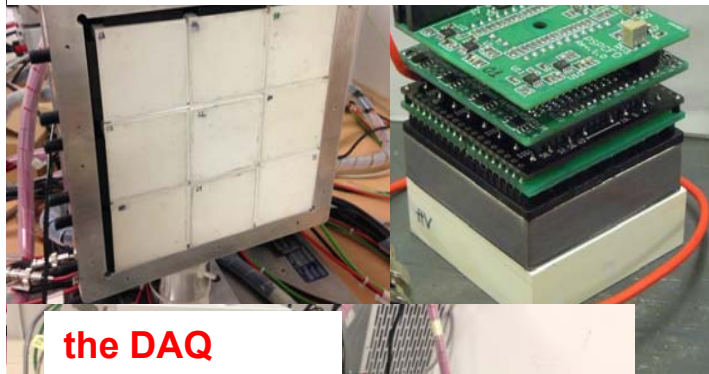


- Capability in beam-on data acquisition
- Advantages of beam-on data: no biological washout, less patient/organ movement, faster patient throughput

DoPET: 15 cm x 15 cm prototype



9 detecting modules the single module



Detecting module 5cm x 5cm

- LYSO matrices, each 23 x 23 crystals, 2mm pitch)
- PS-PMT 8500 Hamamatsu
- Dedicated front-end electronics

- ❖ Modularized acquisition electronics
 - ❖ FPGA based acquisition and coincidence processing
 - ❖ Coincidence time window ~5 ns

➤3D-activity distribution is reconstructed with Maximum Likelihood Estimation Maximization (MLEM) Iterative algorithm

The reconstruction is performed in less than 1 minute (8 core Intel Xeon e5620 @2.4 GHz)

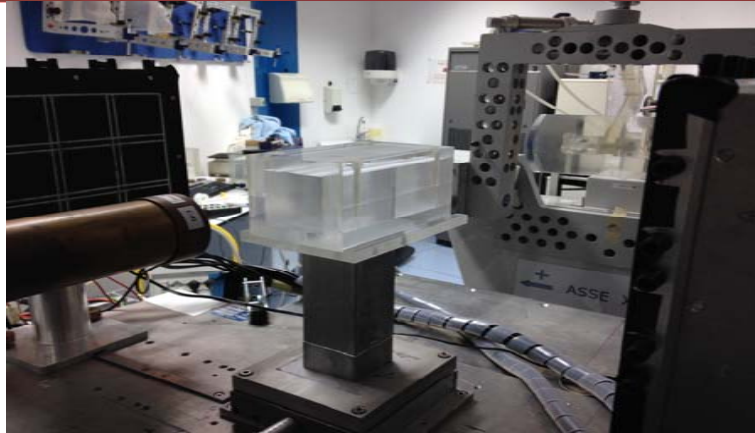
S. Vecchio et al., IEEE Trans. Nucl. Science 56 (2009) 51-56

G. Sportelli et al., IEEE Trans. Nucl. Science 58 (2011) 695-702

N. Camarlinghi et al., JINST 9 (2014) C04005 1-12

Several data taking were performed

CATANA

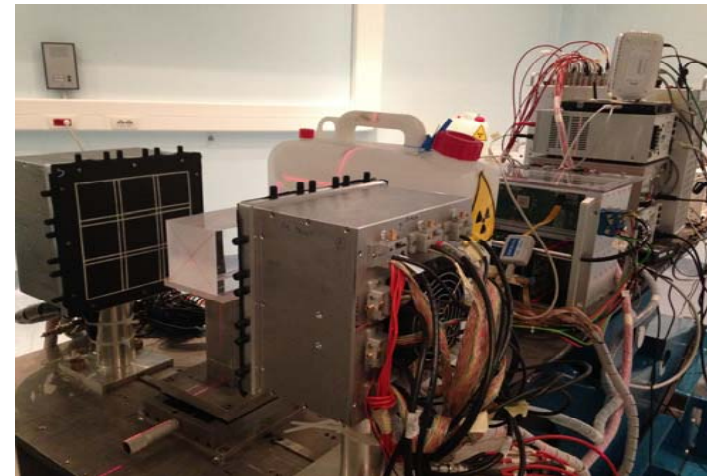


A. Kraan et al., *Physica Medica* 30 (2014) 559-569

V. Rosso et al., *JINST*, 11, C12029 (2016), 1-9

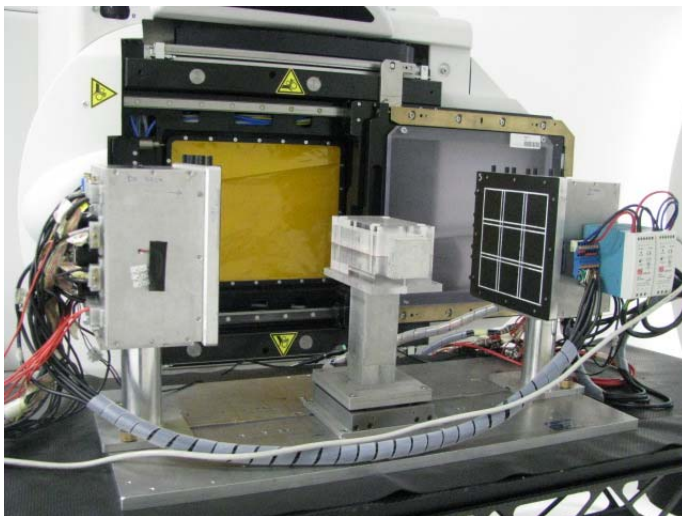
G. Sportelli et al., *JINST*, 10, C12029 (2015) 1-11

V. Rosso et al., *Nucl Instr Meth*, A824, (2016), 228-232



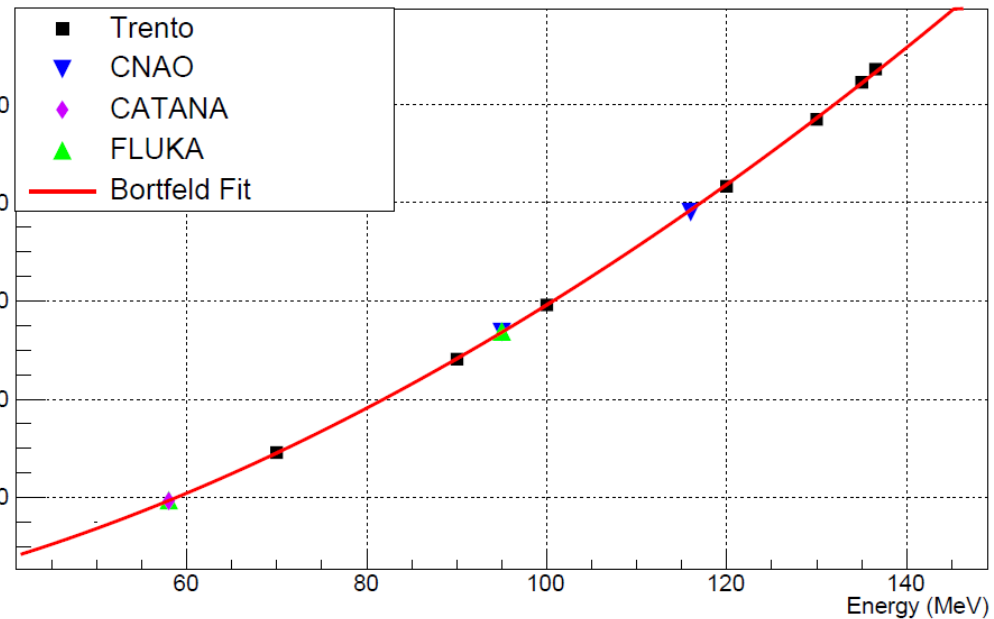
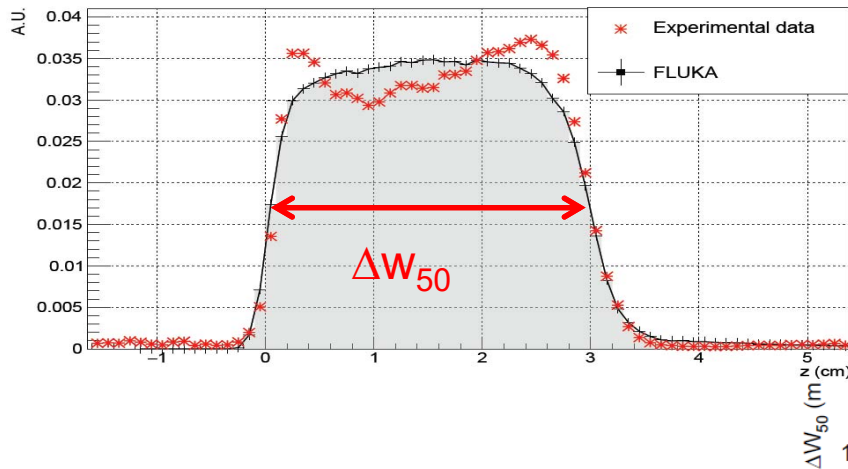
CNAO

TRENTO



Center	Particle	Energy	Accelerator type	Collimation
CATANA	Protons	62 MeV	Cyclotron	passive
CNAO (Pavia)	Protons /C-ions	Up to 230MeV	Synchrotron	active
Trento	Protons	Up to 230Mev	Cyclotron	active

Comparison between measurements taken in the 3 Italian centers

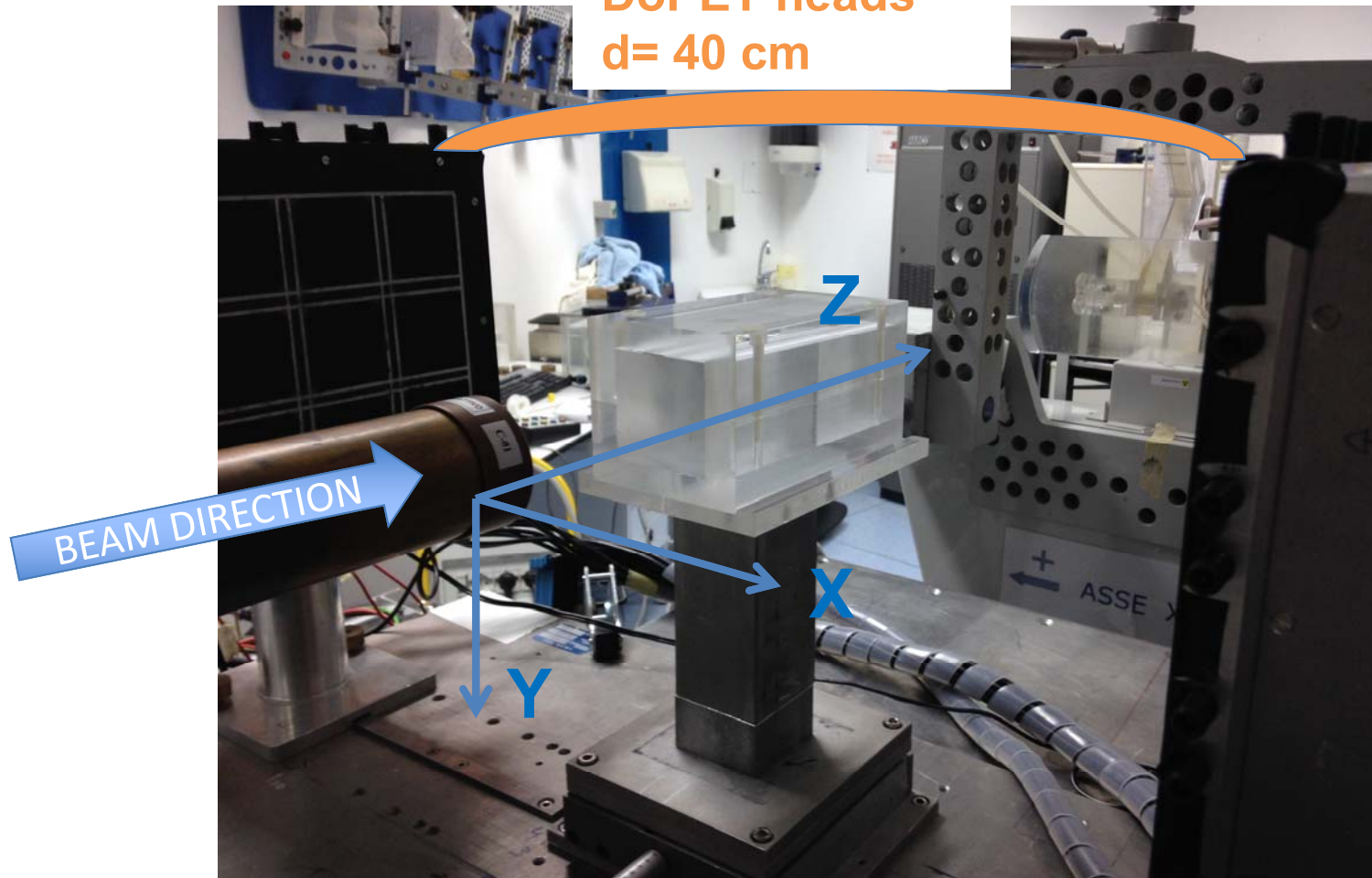


$$\Delta W_{50} = -5,15 + 0.02E_0^{1.77}$$

The data acquired in the 3 Italian proton therapy centers fit well together

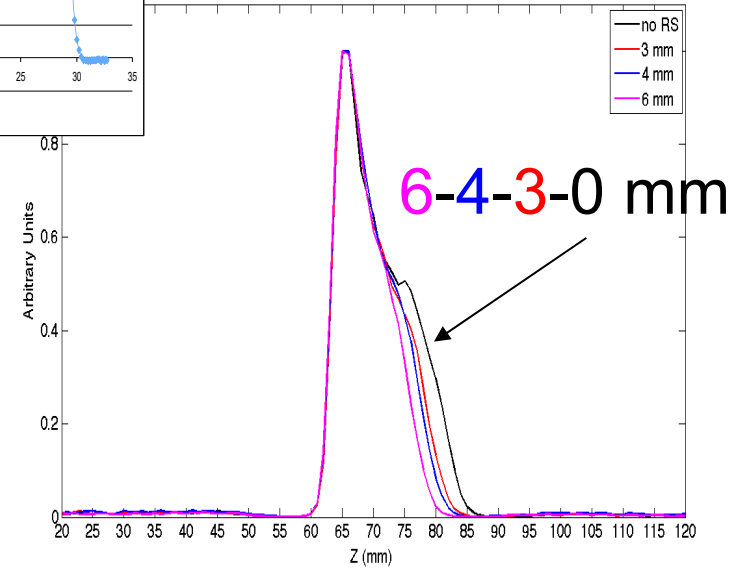
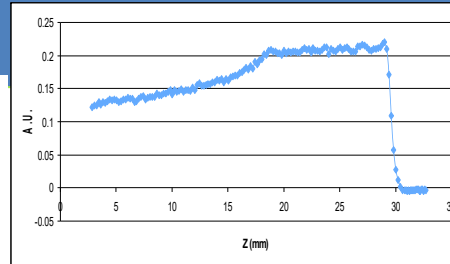
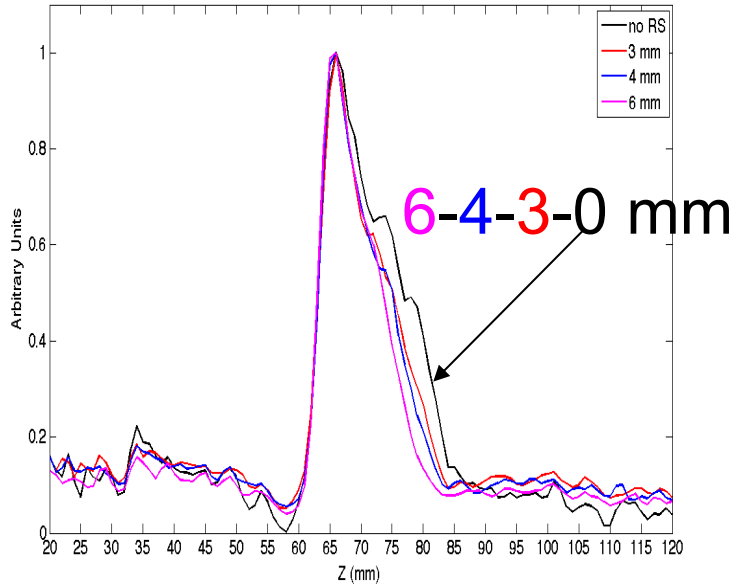
The DoPET system @CATANA

DoPET heads
 $d = 40$ cm



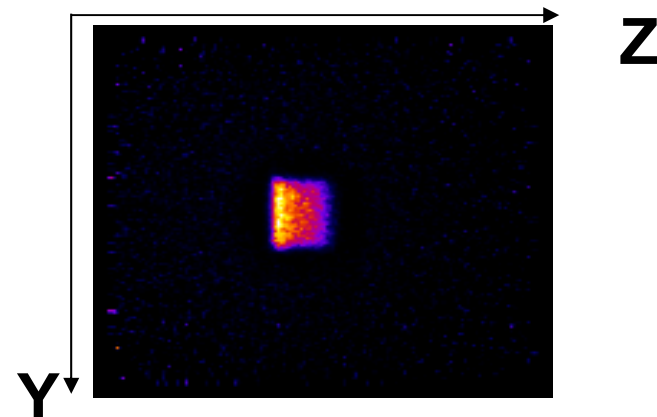
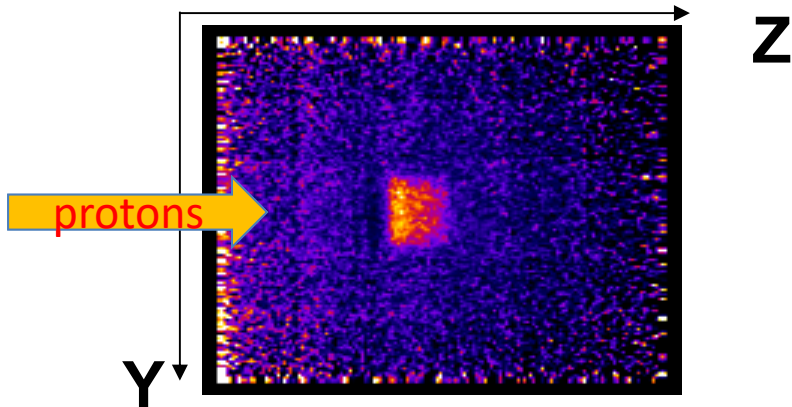
Capability to detect variation in delivered energy

SOBP 2cm, \varnothing 30mm, 15 Gy



in-treatment [0-73 *s]

after-treatment [73*-600s]



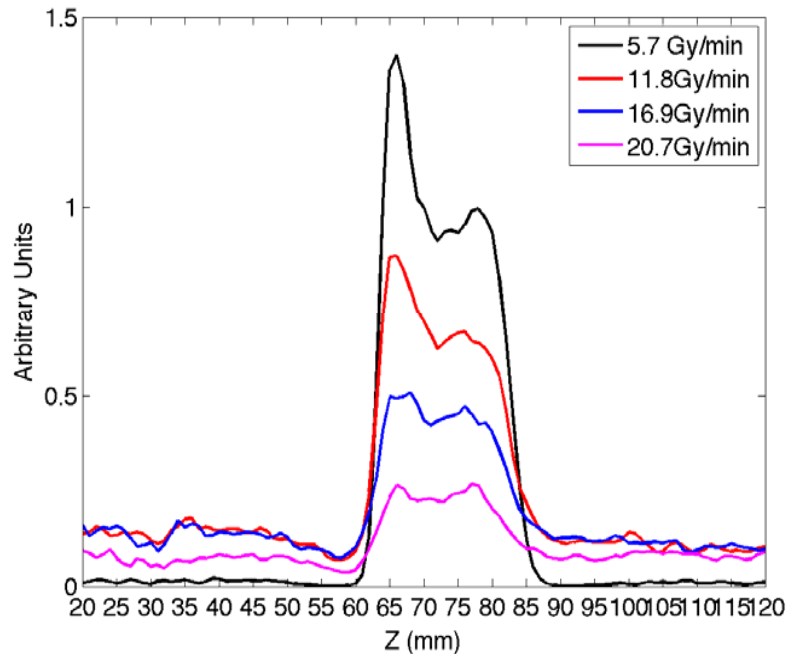
IN-TREATMENT = 73 s no range shifter

AFTER-TREATMENT = 73-600 s no range shifter

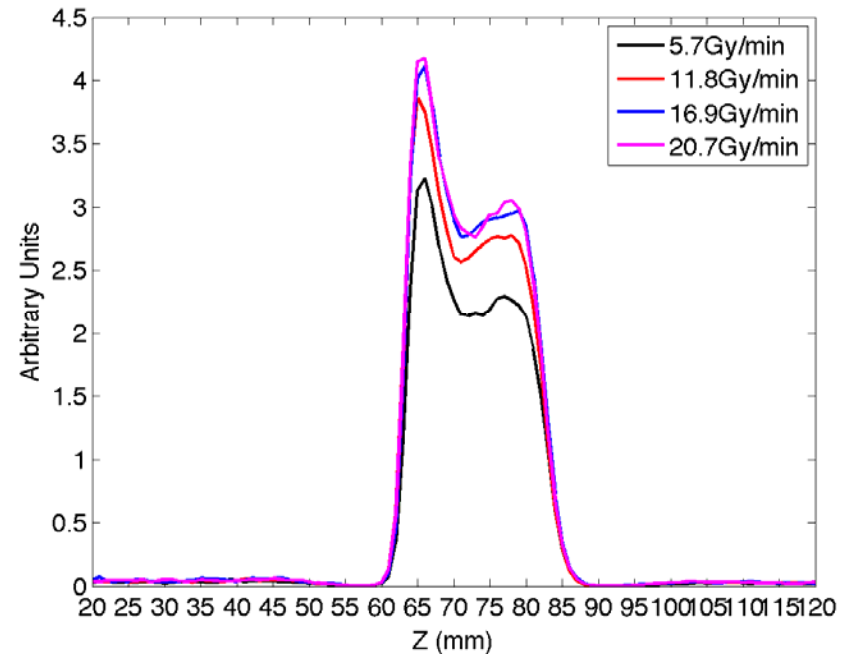
CATANA: response to different dose rates

58MeV protons, \varnothing 30mm, D=15Gy, PMMA

in-treatment activity profiles
 Δt -acq: see table below



after-treatment activity profiles
 Δt -acq: 300 s – 600 s

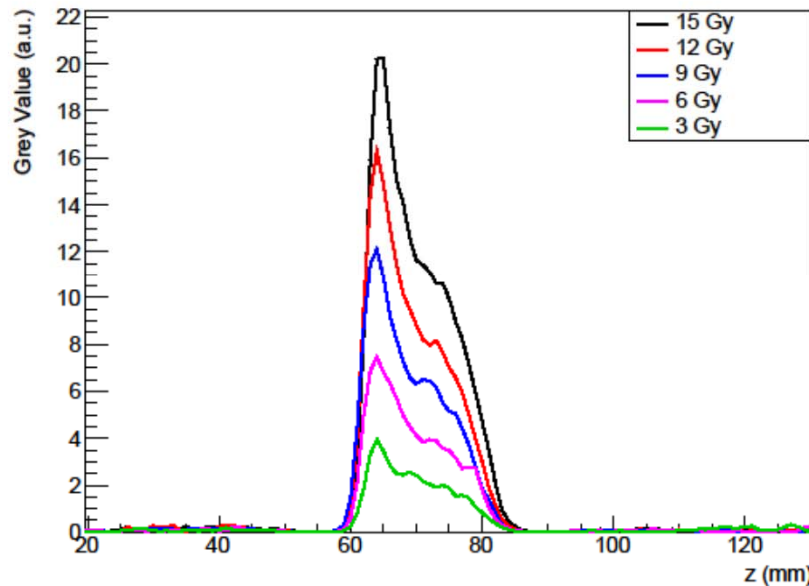


Dose rate [Gy/min]	5.7	11.8	16.9	20.7
Δt -in treatment [s]	157.9	76.5	53.1	43.4

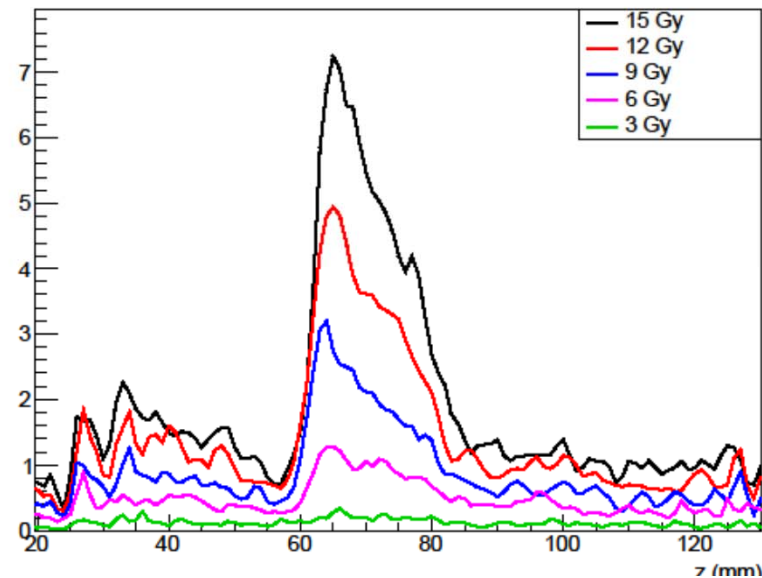
Response to different doses

SOBP 2cm, \varnothing 30mm, ~ 12 Gy/min

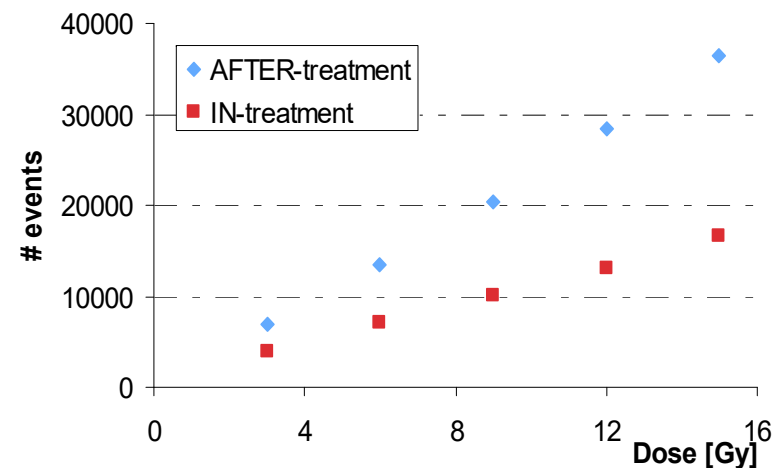
after-treatment [300s-600s]



In-treatment: different Δt see table below

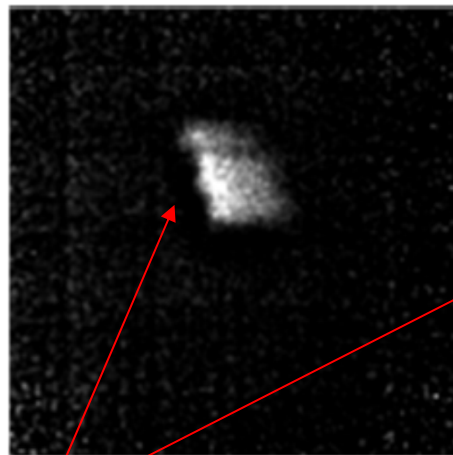
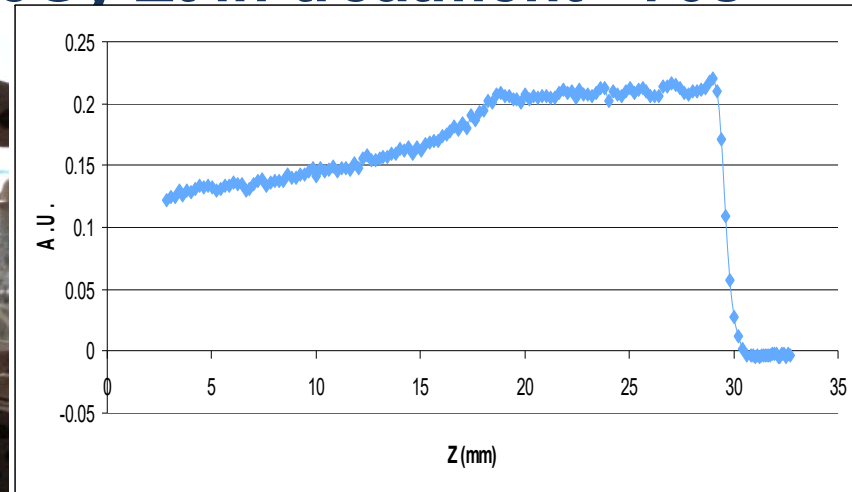
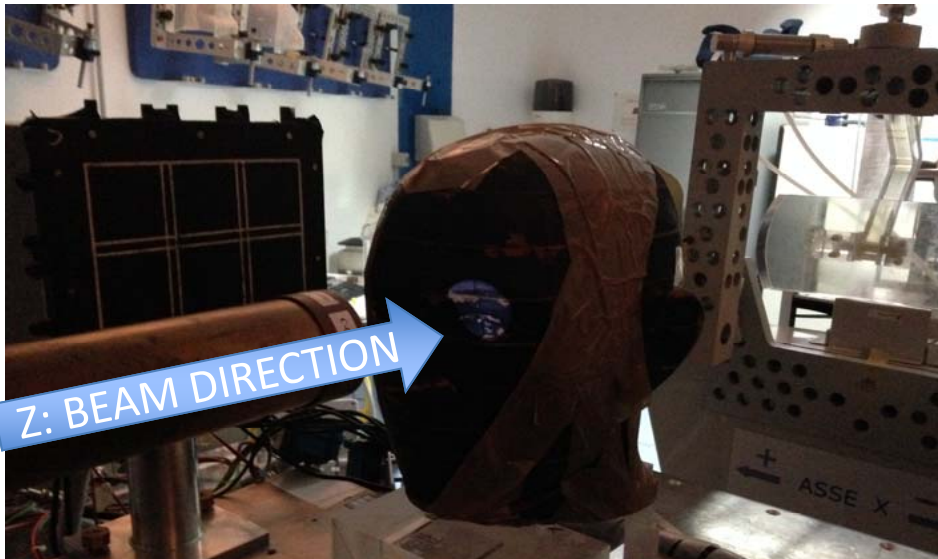


DOSE	Dose-deliver time [s]	Dose/rate [Gy/min]
3 Gy	16.3	11.04
6 Gy	30	12
9 Gy	48	11.25
12 Gy	56.4	12.77
15 Gy	72.9	12.35

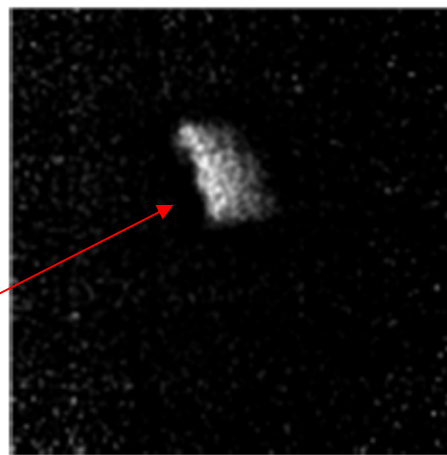


Imaging capabilities using range shifter and an antropomorphic phantom

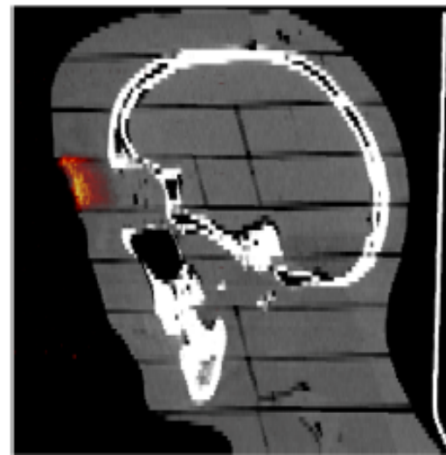
SOBP, collimator: \emptyset 3 cm, D= 15Gy Δt in-treatment= 70s



Phantom eyelid



3 mm range shifter



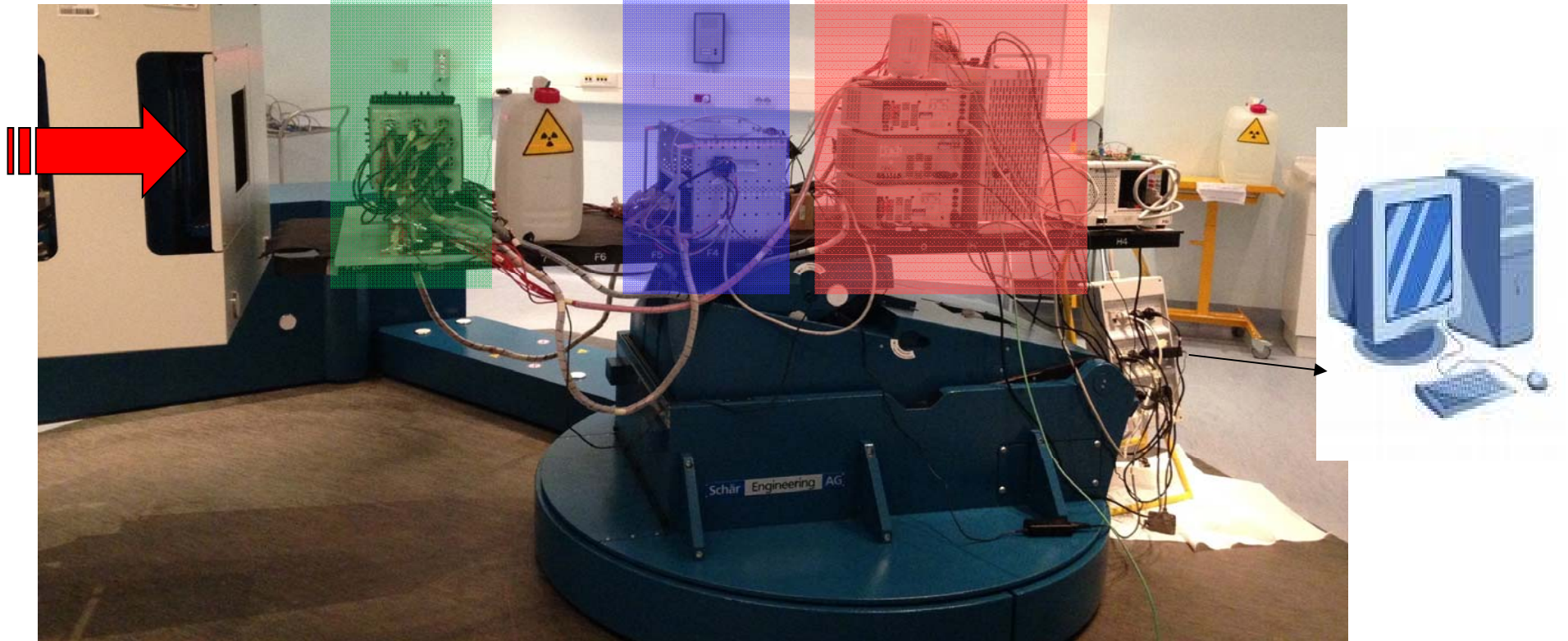
In-and-after
Treatment data:
 Δt -acq= 0-190 s

the DoPET system @ CNAO

detectors

DAQ

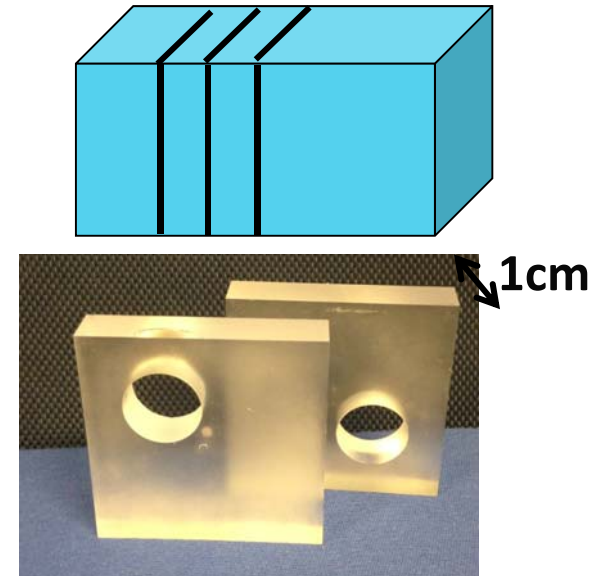
power supplies



CNAO: PMMA phantom with 2 air cavities

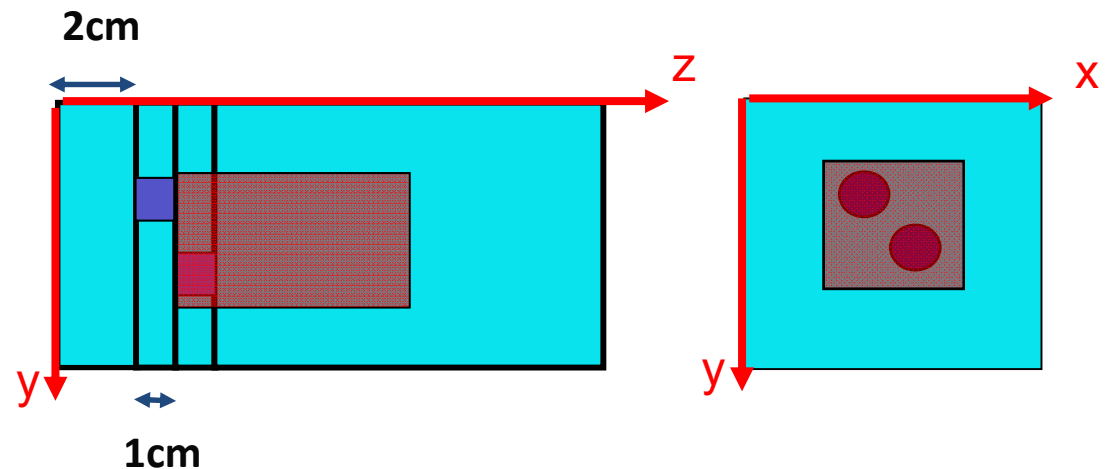
TPS: Syngo PT Planning VC12,
Siemens

- protons
- **2Gy** on PTV: $4 \times 4 \times 6 \text{ cm}^3$ (z: 3-9 cm)
- 62.3 MeV - 116 MeV (35 EL)



Ø 1.6 cm

- PMMA phantom:
 $8 \times 8 \times 14 \text{ cm}^3$
- 2 cavities:
z=1cm
Ø=1.6cm



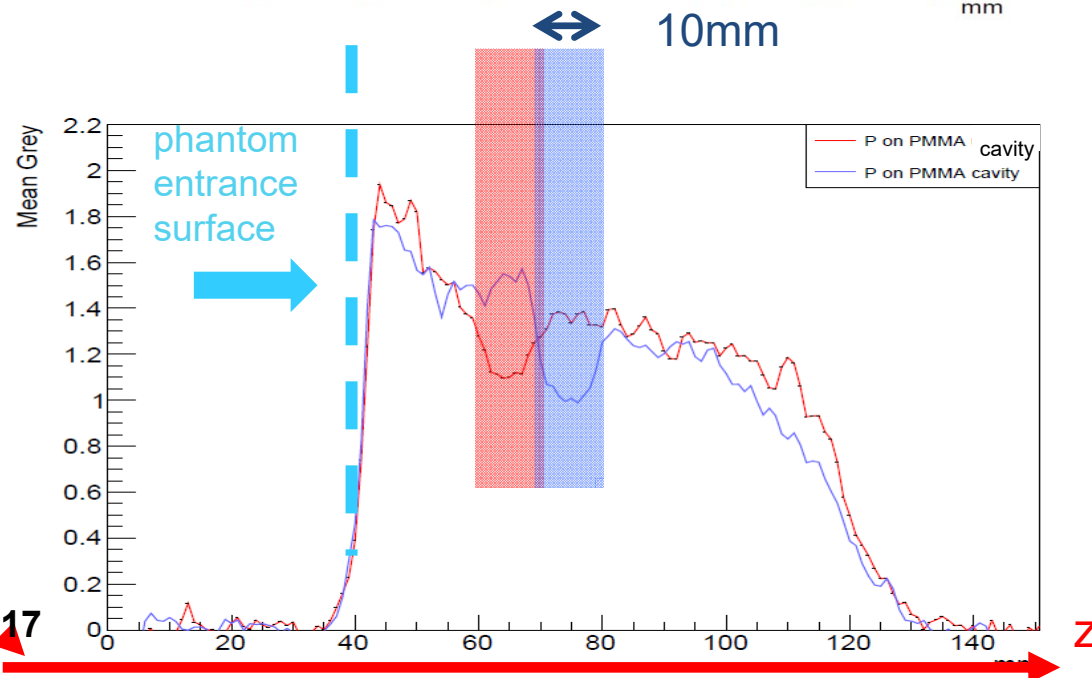
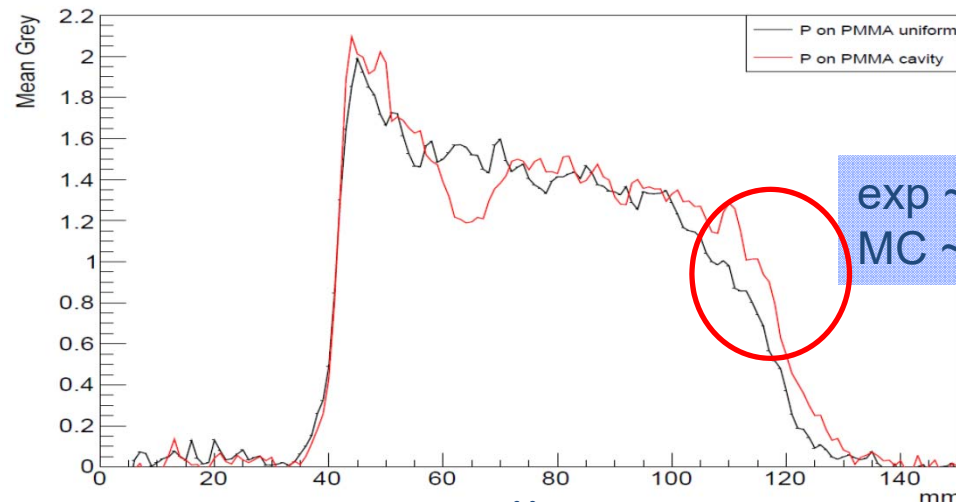
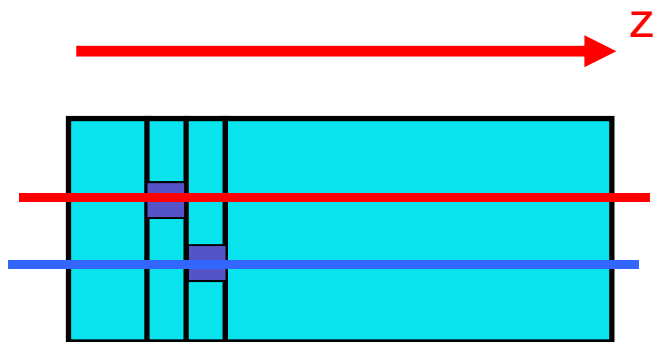
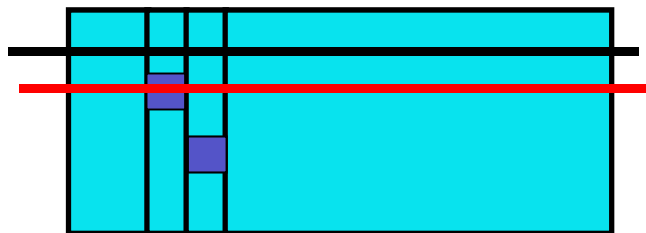
CNAO: 2 cavities profiles

D= 2Gy

Acquisition time [0, 600 s]

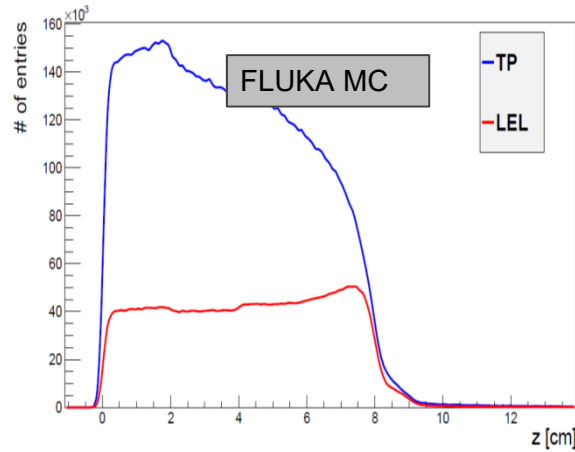
TP delivered in 230 s

Activity: z profile



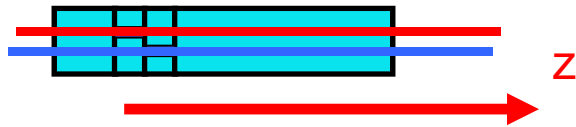
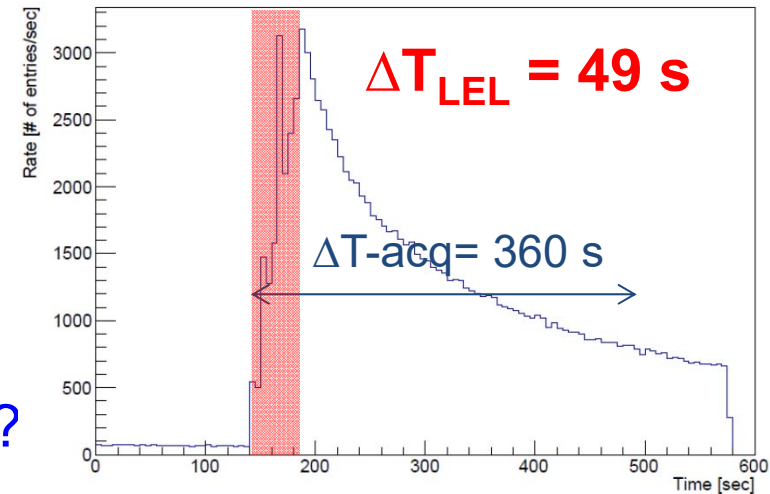
V. Rosso et al.,
<http://dx.doi.org/10.1016/j.nima.2015.11.017>

CNAO: Last Energy Layer

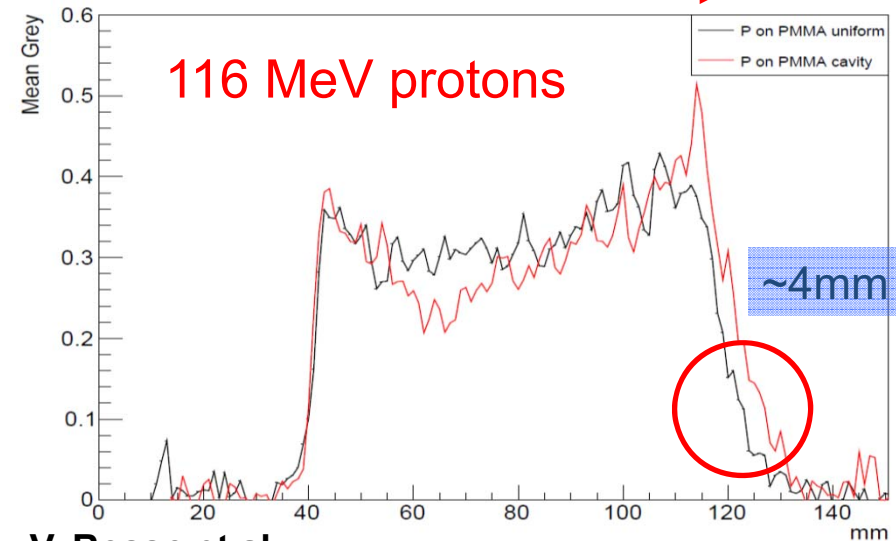
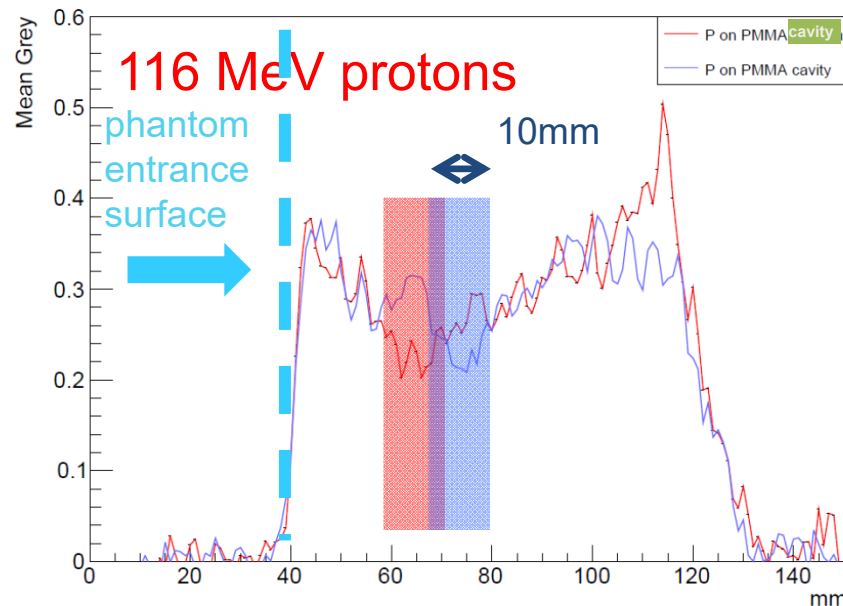
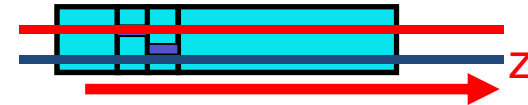


only LEL protons

The same information with a smaller dose: helpful for hypofractionation?



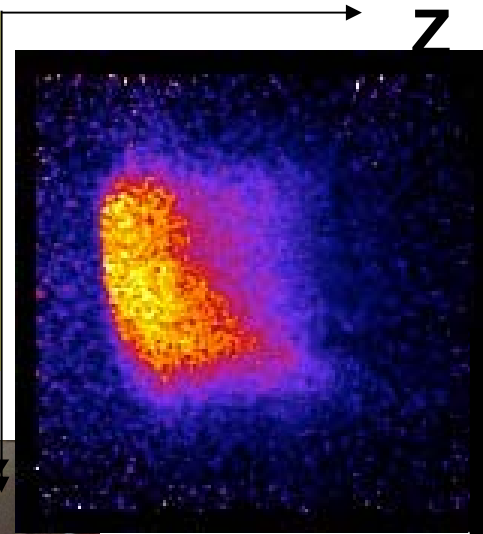
$\Delta T\text{-acq} = 360 \text{ s}$



V. Rosso et al.,
<http://dx.doi.org/10.1016/j.nima.2015.11.017>

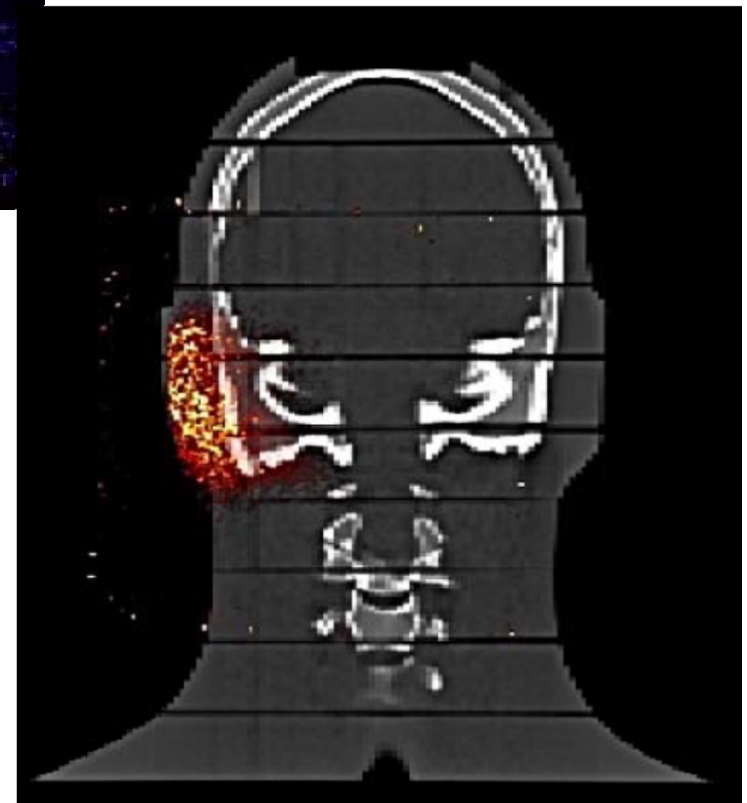
CNAO: an example of an antropomorphic phantom irradiation

2 Gy on PTV: 5x5x6
cm³ (z: 1-7 cm)
 Δt in-treatment= 287s



Acquisition time
[0, 600 s]

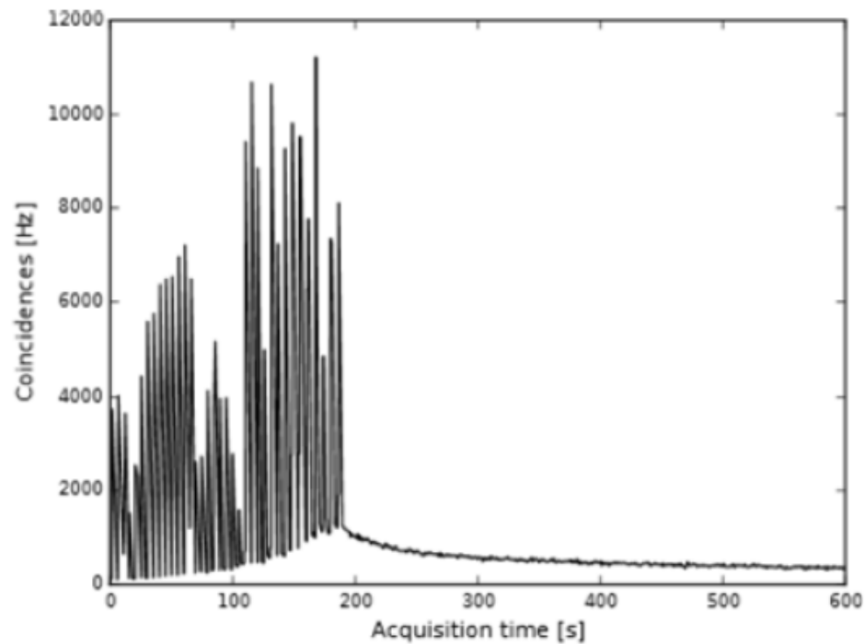
coronal view



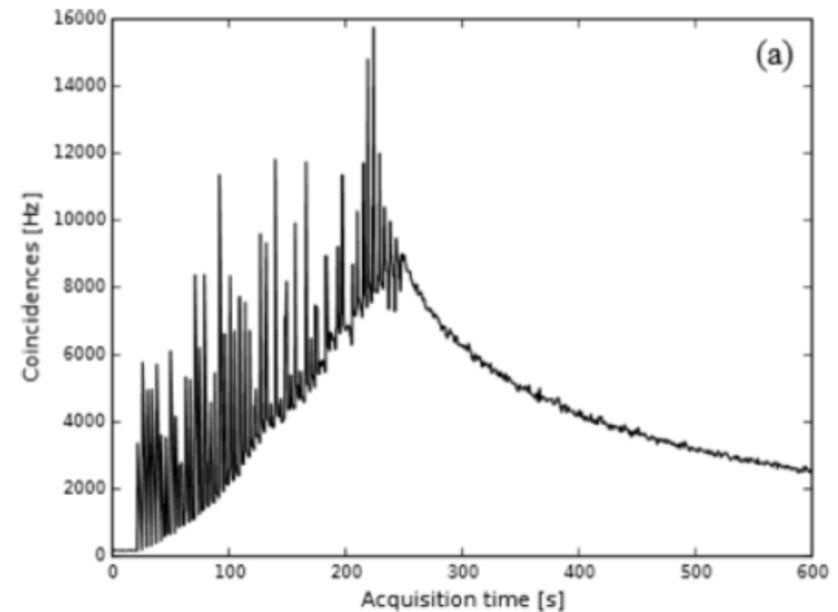
CNAO: proton and carbon irradiations

2 Gy on PTV: 4x4x6
cm³ (z: 3-6 cm)

Carbon TP

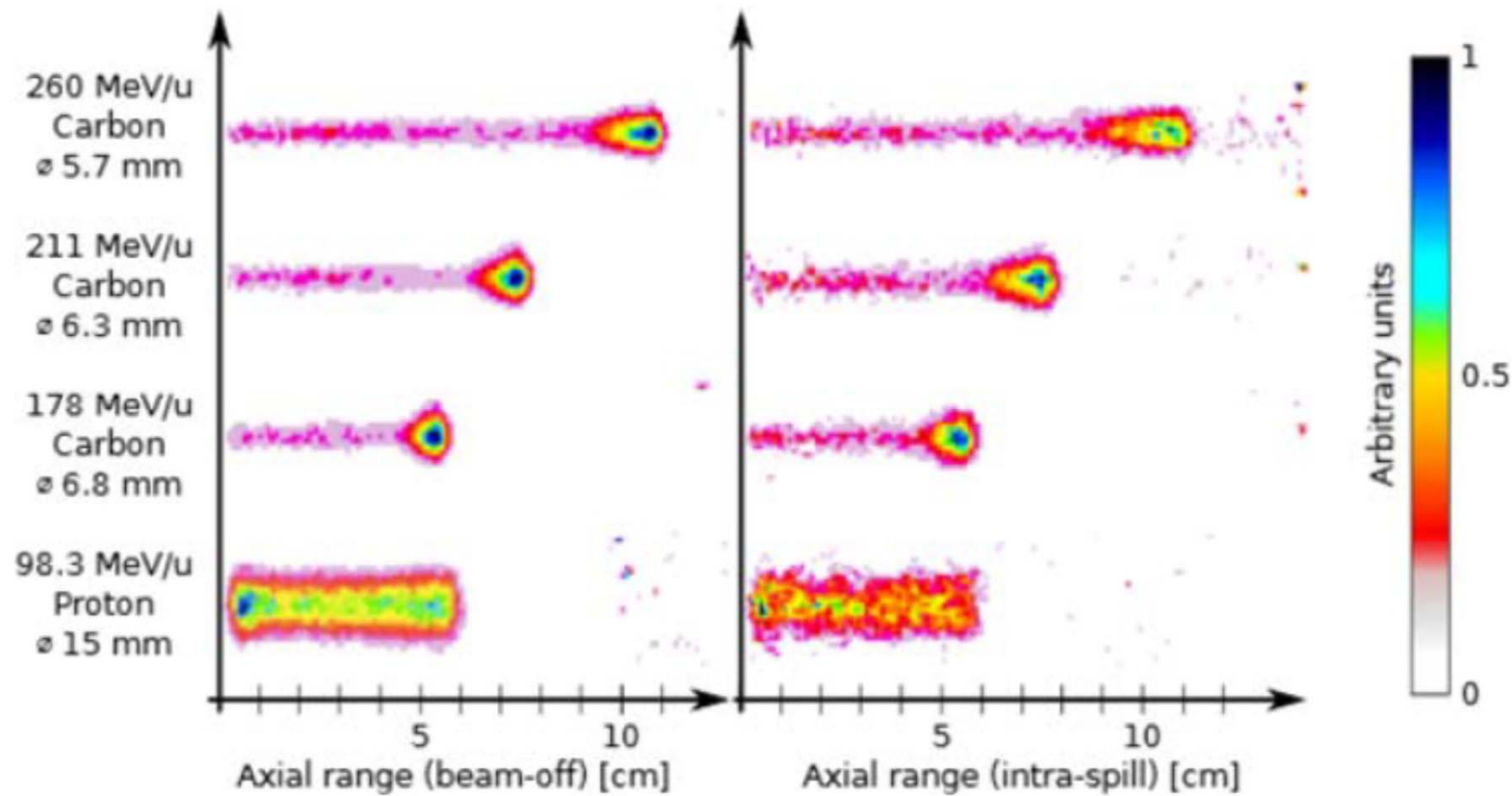


Proton TP

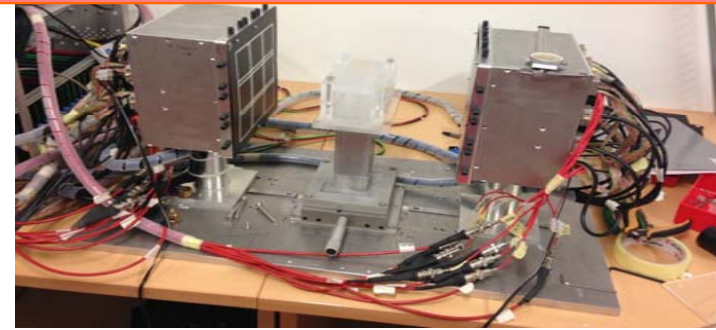
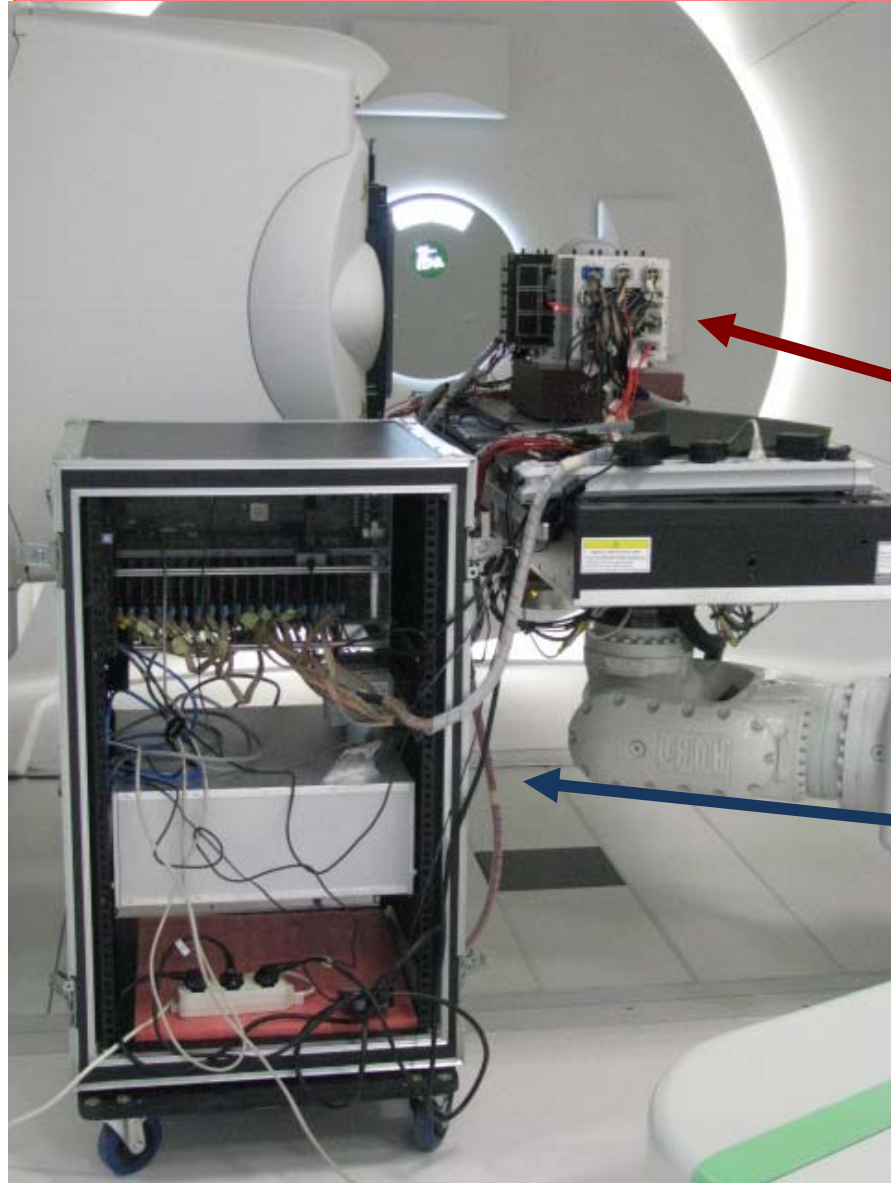


Different statistic...

CNAO: carbon and proton monoenergetic irradiations



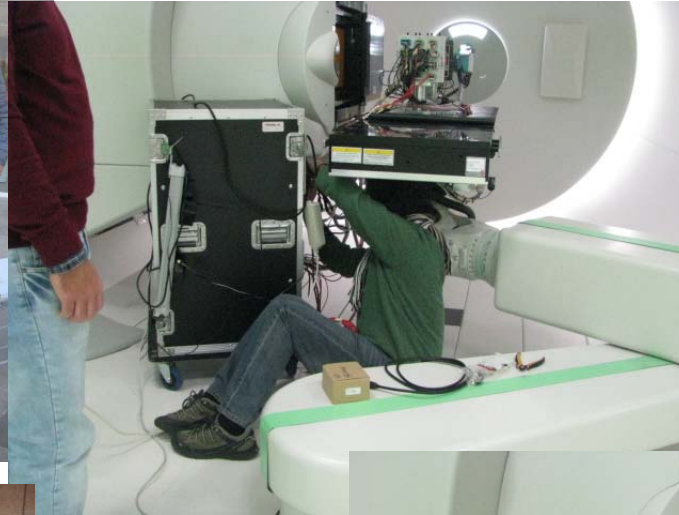
the DoPET system @ Trento



The 2 detecting heads

The fly-rack: a compact housing for the DAQ and the power supplies

the DoPET system @ Trento



Ready for data taking in 30' !

Capability to detect variations in composition

	Densita'	H (%)	C (%)	O (%)	N (%)	Ca (%)
PMMA	1.18	8	60	32		
Solid H2O	1.046	8.02	67.23	19.91	2.41	2.31
brain	1.049	10.83	72.54	14.86	1.69	
polyethylene		14	86			

3 “zebra” phantoms were realized:

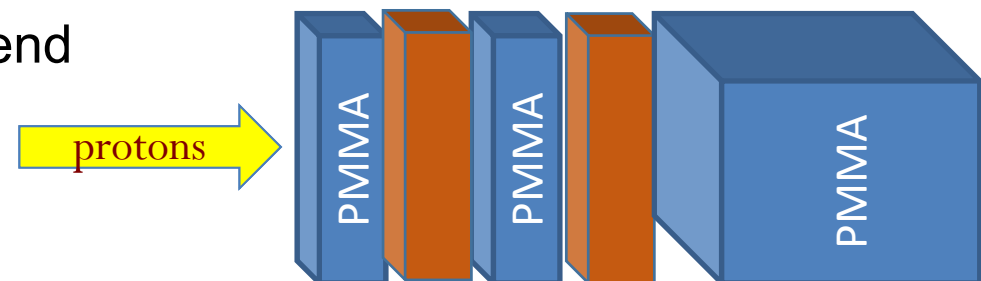
I) PMMA-PE-PMMA-PE-PMMA –to-end

II) PMMA-BRAIN-PMMA-BRAIN-PMMA —to-end

III) PMMA-H2O-PMMA-PMMA —to-end

Slabs thickness: 2cm

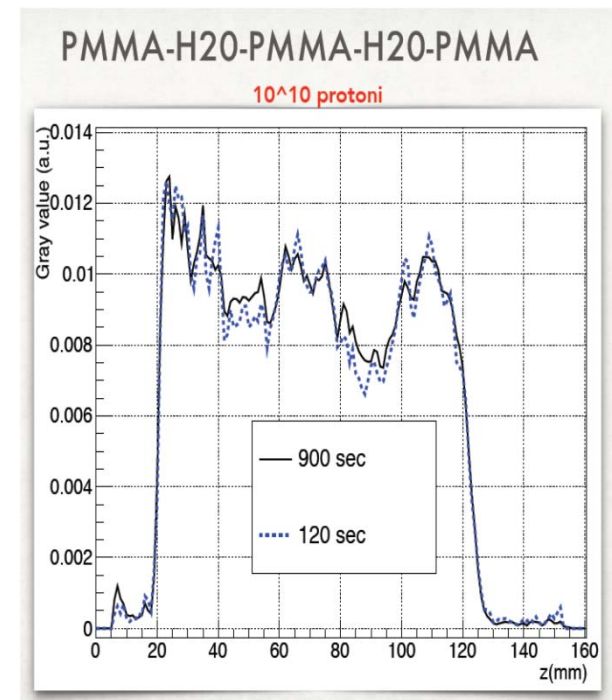
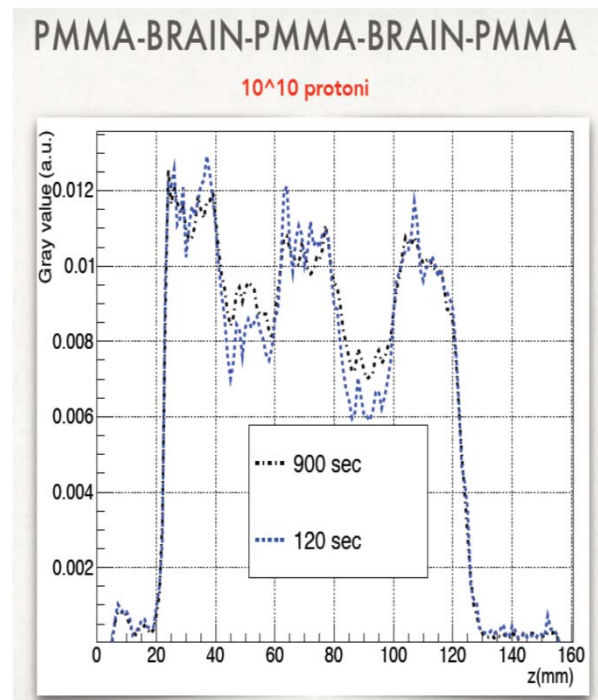
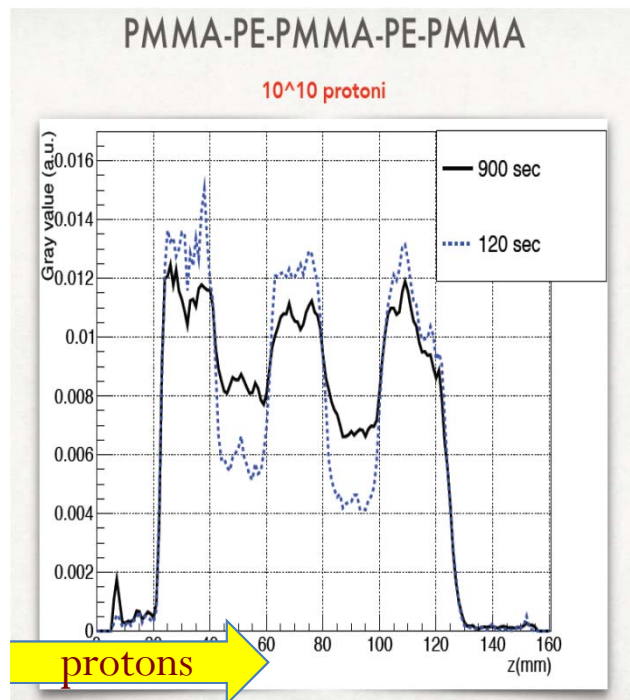
Phantom thickness:14cm



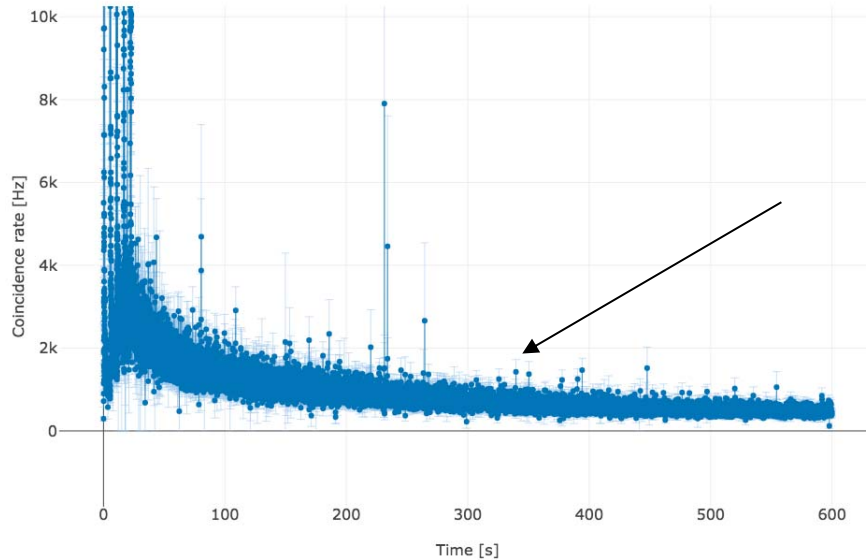
Capability to detect variations in composition Zebra-phantoms profiles

Pencil beam: energy 130MeV , 10^{10} protons

Different acq. time to enhance the contribution of the 15O and 11C isotopes (120 and 900s)



Capability to detect variations in composition: a time approach

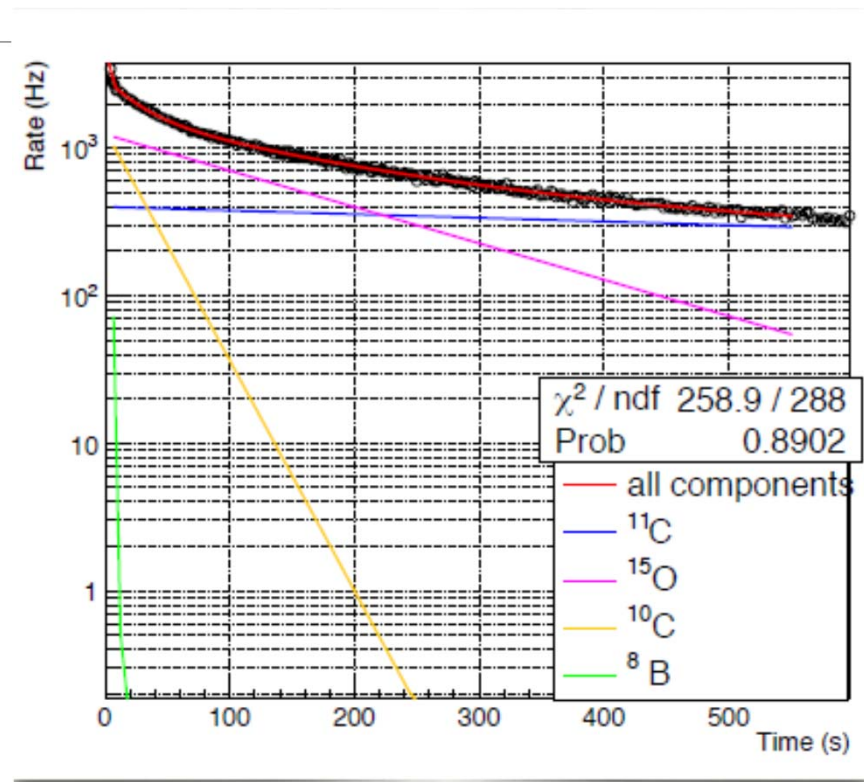


Evaluate the different contributions knowing the isotopes: ^{11}C , ^{15}O , ^{10}C , ^8B and ^{13}N

The contributions of the different isotopes was calculated, modeling the frequency signal as:

$$f(t) = \sum_{i=1}^n a_i e^{-t \ln 2 / T_i}$$

$$\Delta T\text{-acq} = 550\text{s}$$



Capability to detect variations in composition: a time approach

isotopes	11-C (%)	15-O (%)	10-C (%)	8-B (%)
PMMA	39.7±0.3	52.2±0.4	7.8±0.1	0.24±0.02
H2O solid	51.4±0.3	37.4±0.4	10.0±0.2	1.15±0.03
BRAIN	58.6±0.4	29.3±0.4	11.8±0.2	0.34±0.03
PE	81.9±0.3	0	17.1±0.1	0.98±0.04
PMMA-H2O	44.8±0.3	46.7±0.4	8.2±0.2	0.28±0.14
PMMA-BRAIN	46.9±0.3	43.6±0.4	8.8±0.2	0.68±0.24
PMMA-PE	52.0±0.3	37.1±0.4	10.5±0.1	0.38±0.03

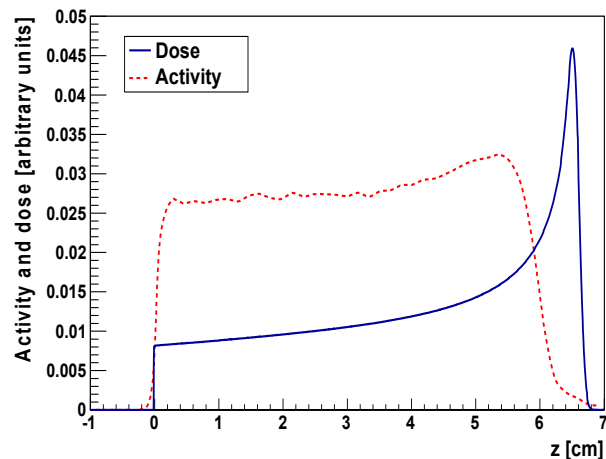
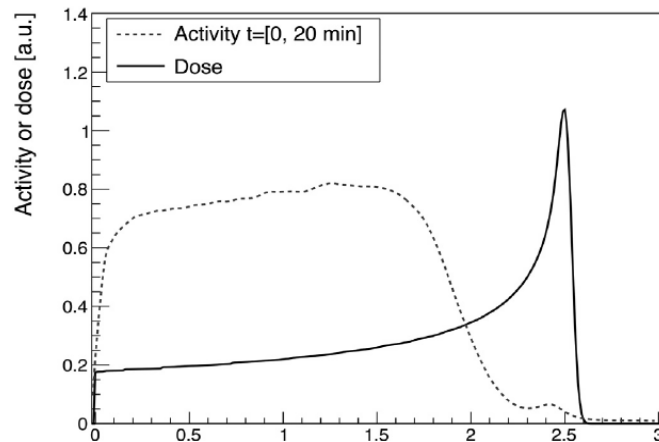
The percentage of the different contributions highlights the different composition

Only 4 cm in thickness are different from one phantom to the other

Expected profiles: FLUKA and comparison with experimental data

As the relation between activity and dose is indirect

58 MeV protons on PMMA



95 MeV protons on PMMA

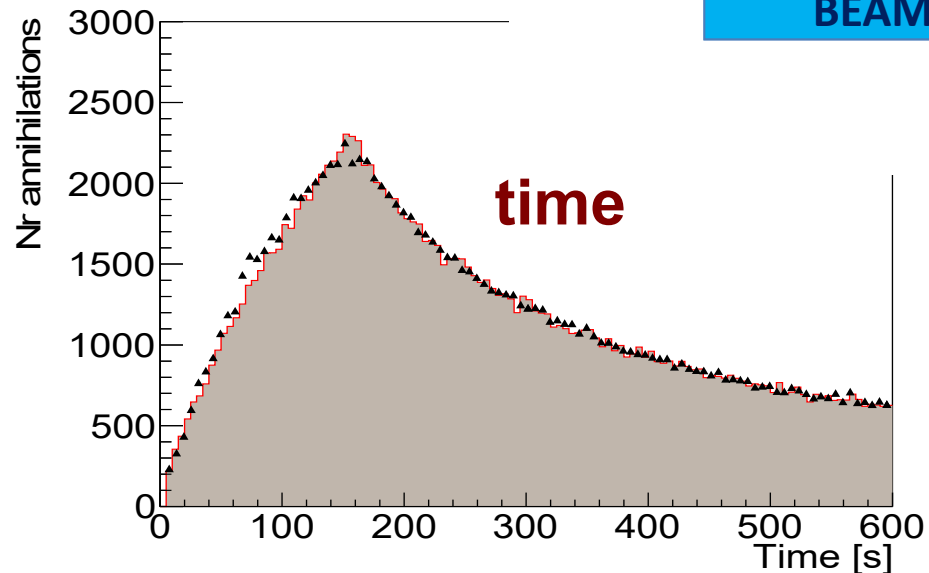
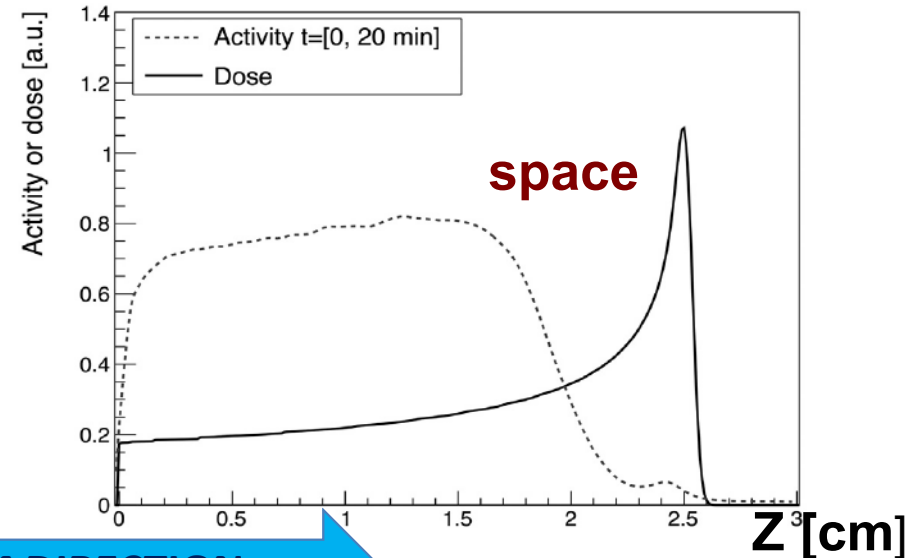
...by comparing predicted with planned activity, the treatment quality can be monitored

Monte Carlo:

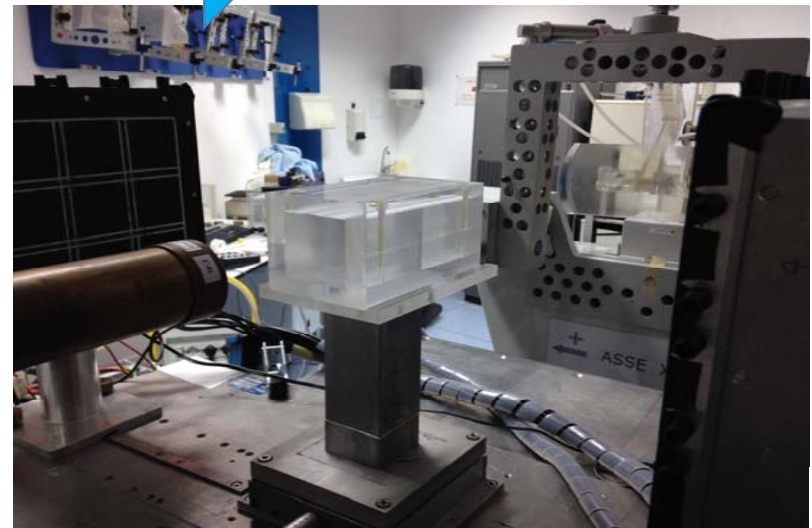
FLUKA (development), new user interface developed to record the β^+ -activity and annihilation products in space and time

CATANA: expected activity profiles (FLUKA MC)

- **58 MeV protons on PMMA (ocular melanoma)**
- **collimator: \varnothing 30mm**
- **D= 15 Gy**
- **in-treatment: 0-158s (5.7 Gy/min)**
- **after-treatment: 158s-300s**
- ❖ Simulations with FLUKA
<http://www.fluka.org>



Annihilation Time profile



CATANA: comparison between simulated and experimental data

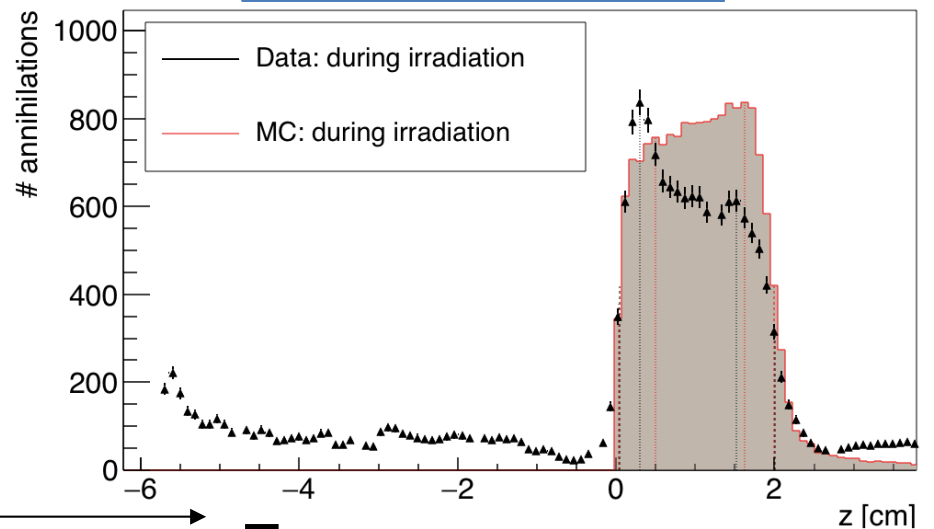
- 58 MeV protons on PMMA
- collimator: \varnothing 30mm
- D= 15 Gy (5.7 Gy/min)

58MeV protons: Z axis

PMMA

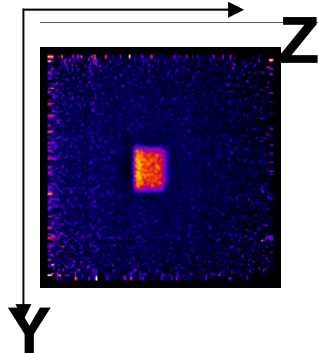
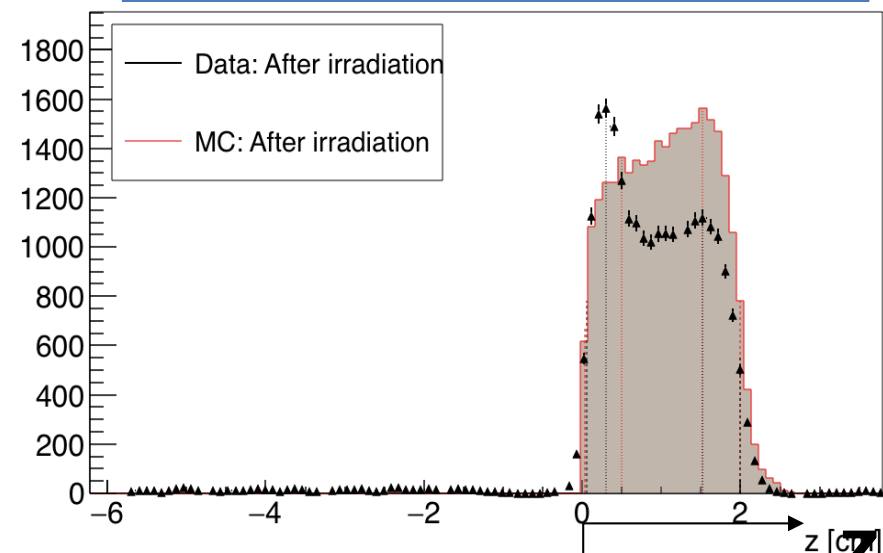
z-profile

In-treatment: $t < 158$ s

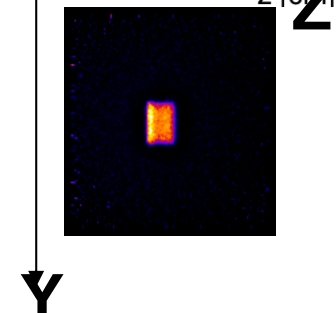


z-profile

After treatment: 158s-280 s



$\Delta w_{50\%}$	in-treatment [cm]	after-treatment [cm]
MC	1.96	1.96
data	1.95 ± 0.03	1.93 ± 0.03

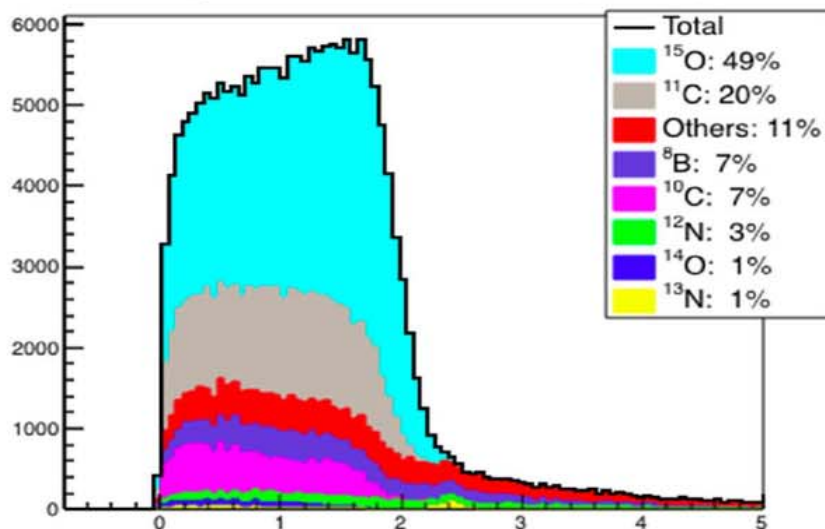


CATANA: expected activity profile (FLUKA MC)

- 58 MeV protons on PMMA
- collimator: \varnothing 30mm
- D= 15 Gy (5.7 Gy/min)
- in-treatment: 0-158s
- after-treatment: 158-300s

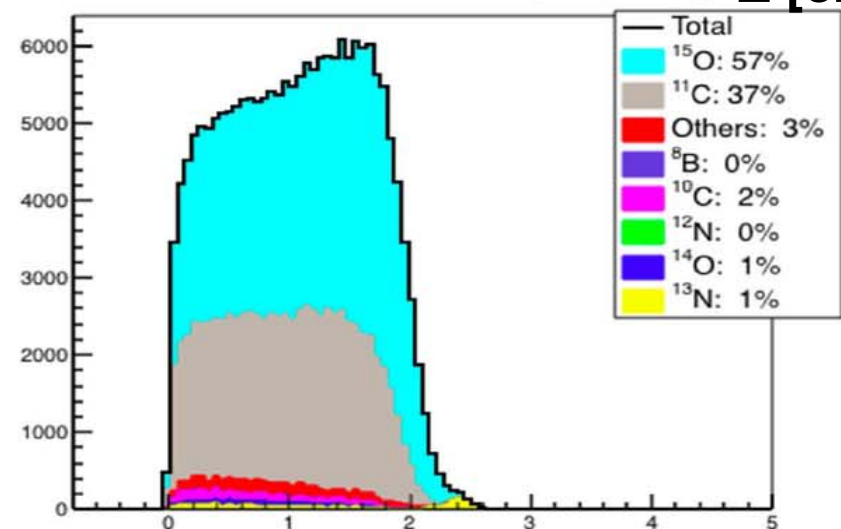
BEAM DIRECTION

During irradiation contribution: t =[0, 158 s]



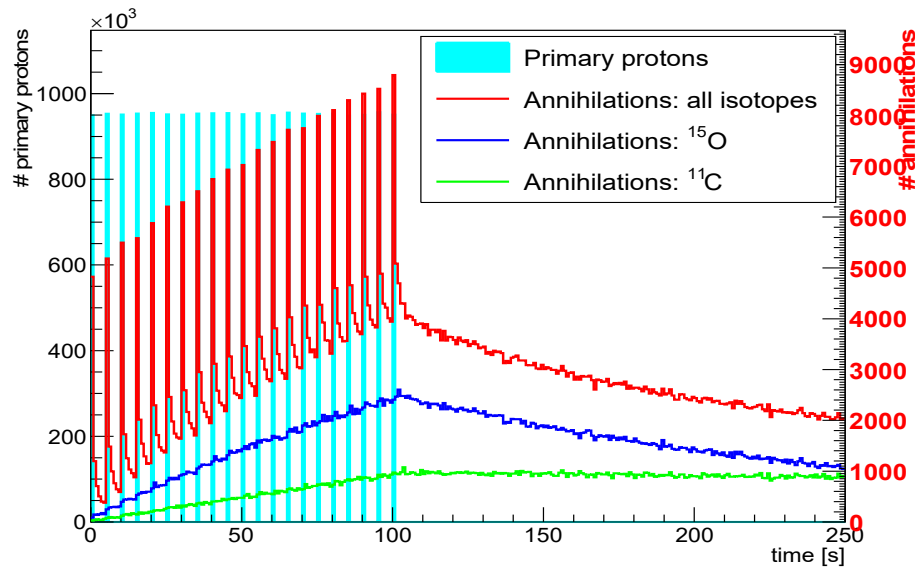
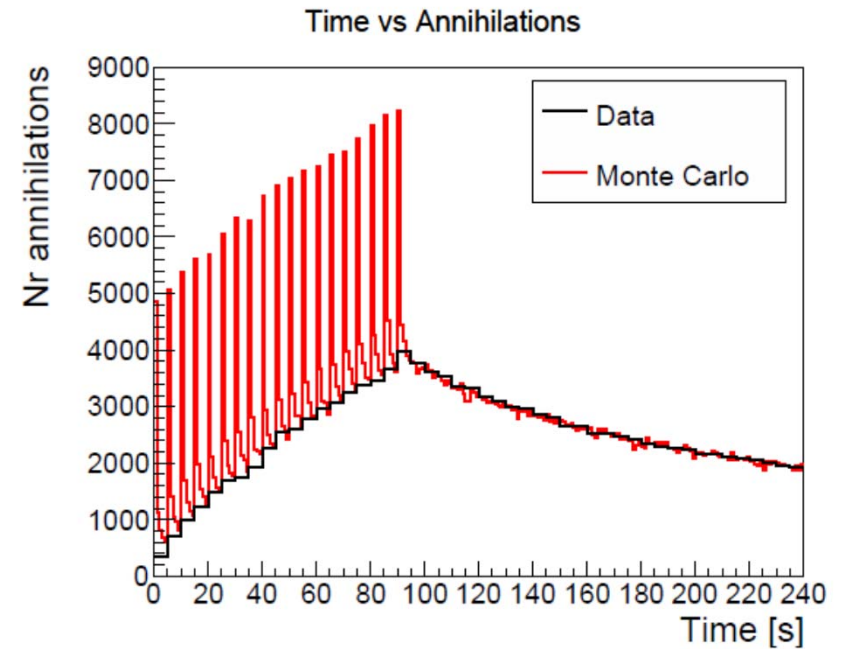
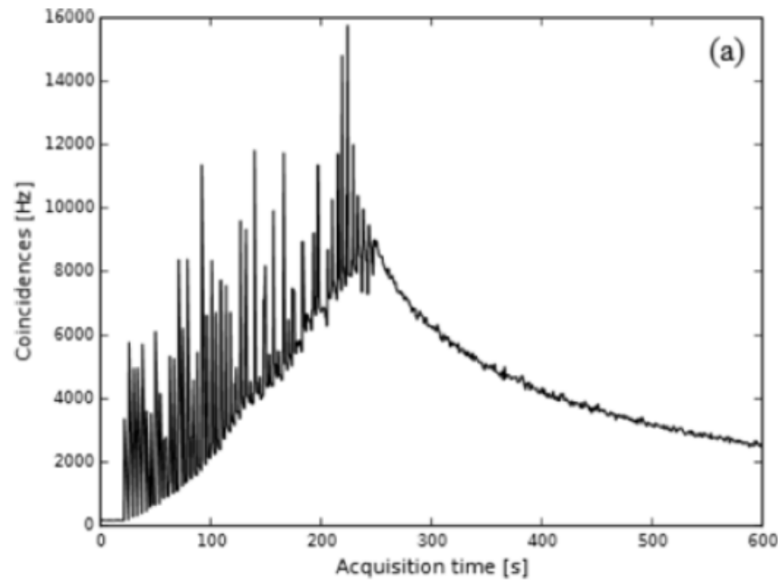
in-treatment activity profile Z [cm]

After beam contribution: t =[158, 300 s] Z [cm]



after-treatment activity profile Z [cm]

FLUKA for CNAO data



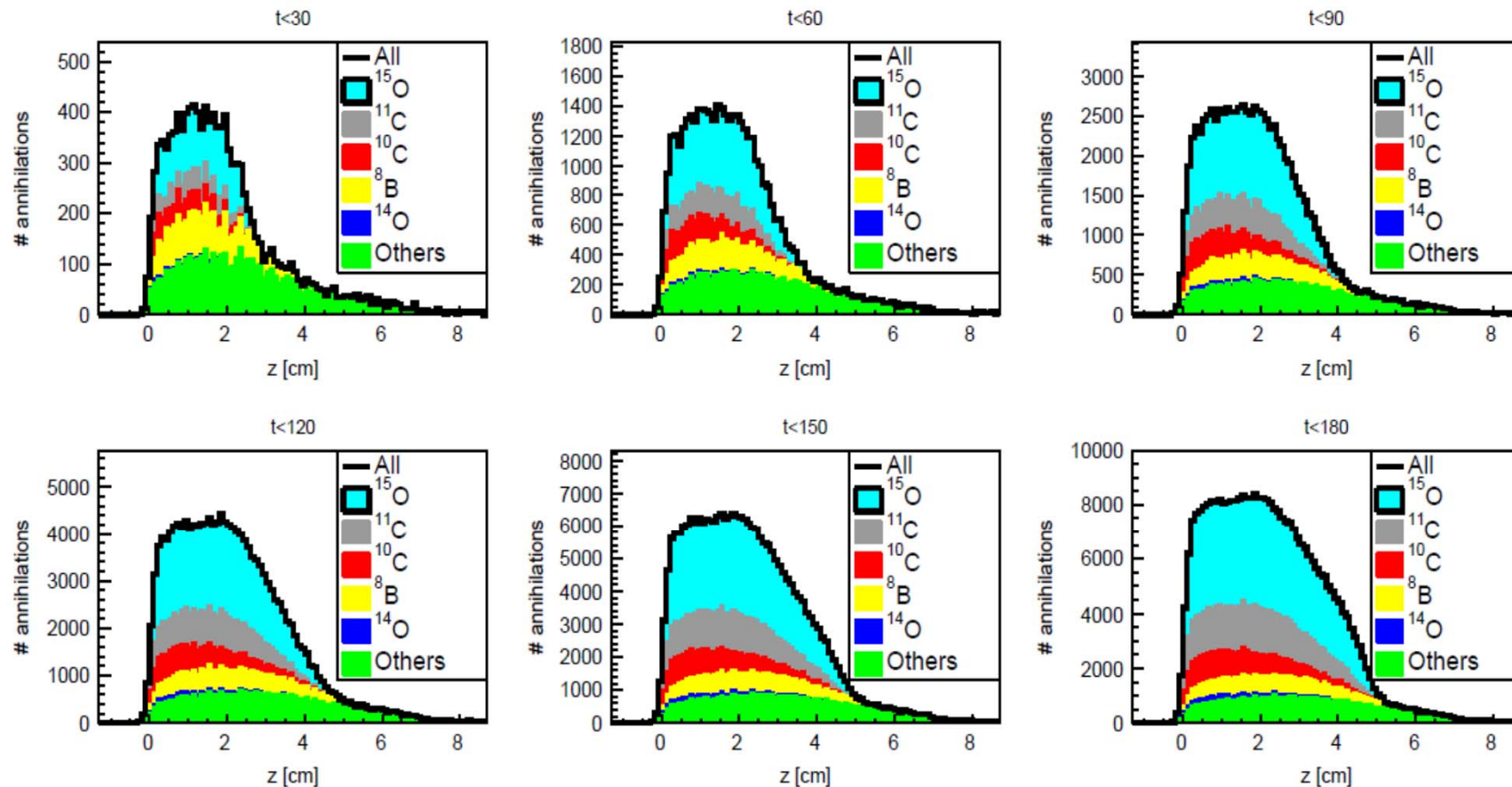
several information are available

CNAO: an example of expected profiles and isotopes contribution

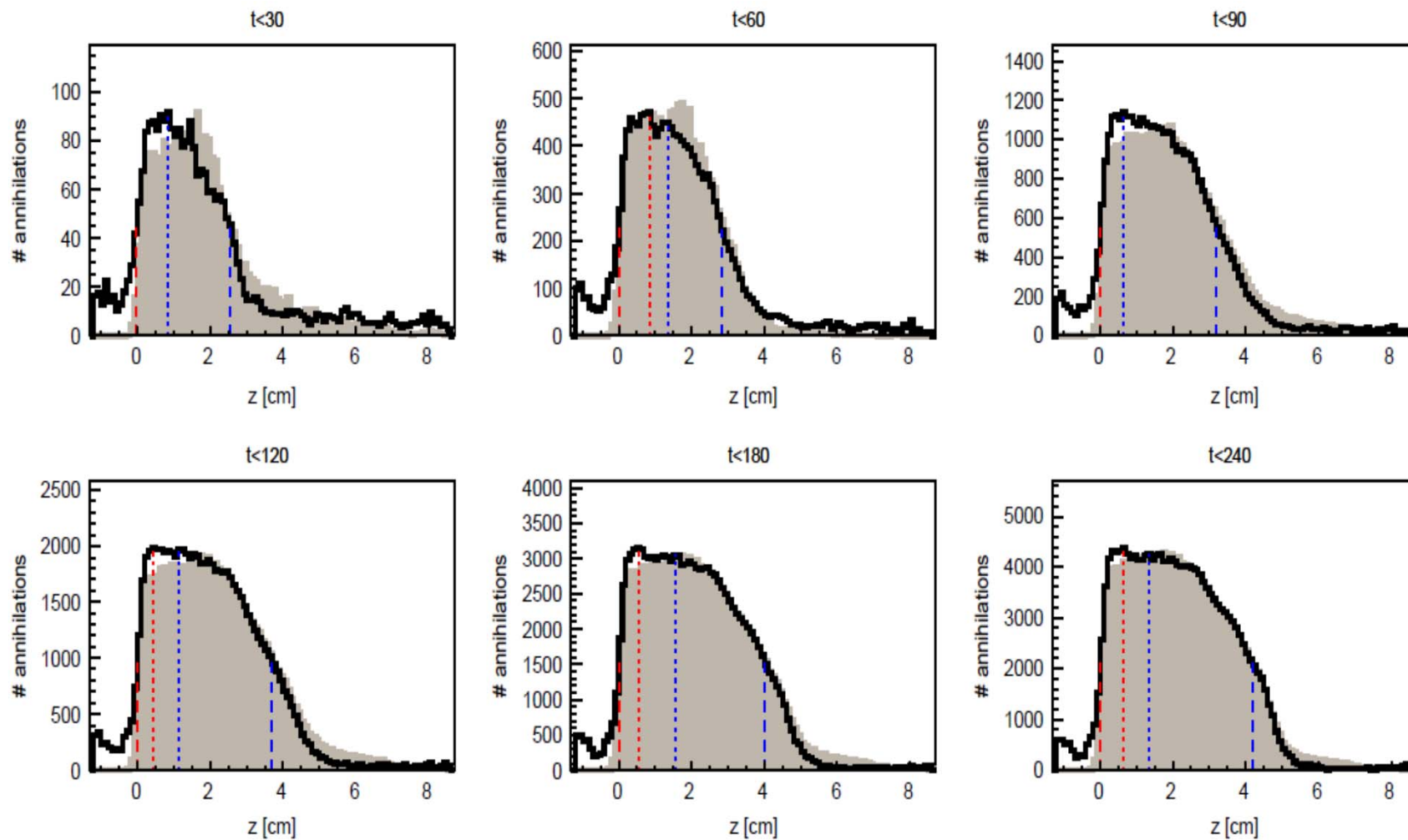
Protons on PMMA

2 Gy on PTV: $3 \times 3 \times 3 \text{ cm}^3$ (z: 3-6 cm)

T-irradiation: 146 s



CNAO: an example of comparison between expected and experimental profiles

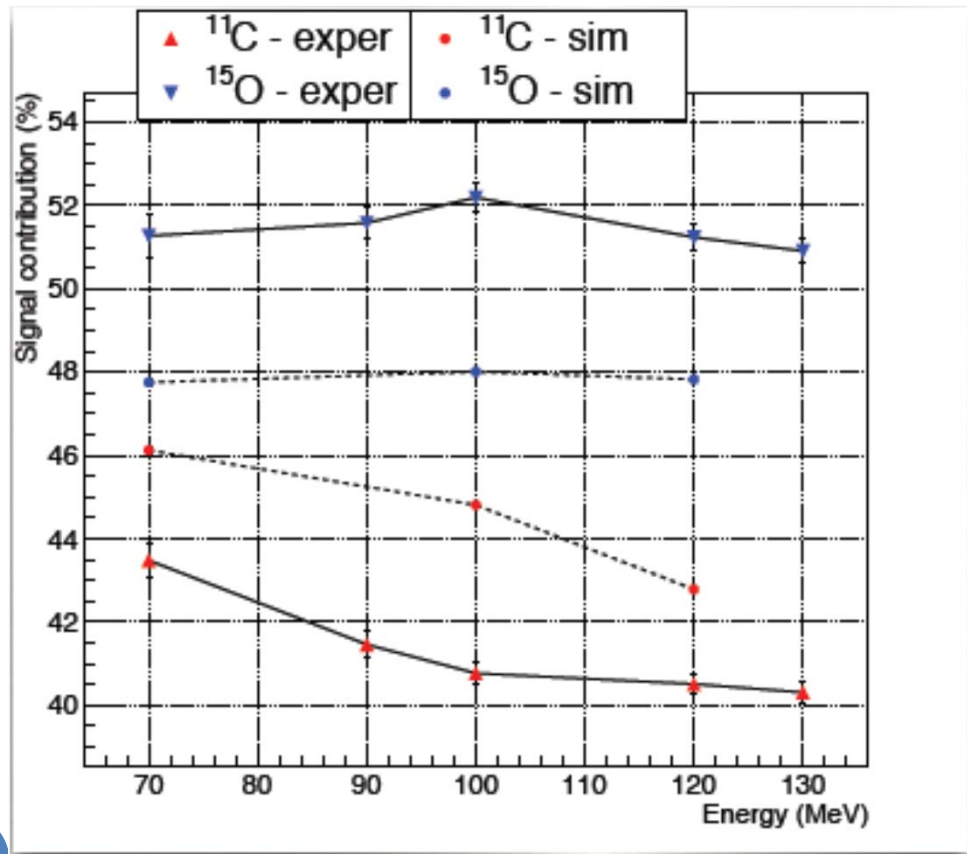


FLUKA for Trento data

Comparison for proton irradiation

Data: 70 MeV, 90 MeV, 100 MeV, 120 MeV and 130 MeV

FLUKA: 70 MeV, 100 MeV and 120 MeV



Work in progress!

PUBBLICAZIONI

- 1) K. Straub et al., Study of UT glasses for pixel identification performance in multi-anode PMT-based detectors for PET
Nuclear Instruments and Methods in Physics Research A718 (2013)154–156
doi:10.1016/j.nima.2012.08.101
- 2) G. Sportelli et al., Full in-beam PET measurements of 62 MeV protons onto a PMMA target
Nuclear Instruments and Methods in Physics Research A 718 (2013) 151–153
doi:10.1016/j.nima.2012.08.100
- 3) V. Rosso et al., A new PET prototype for proton therapy: comparison of data and Monte Carlo simulations
Journal of Instrumentation 8 C03021 (2013) 1-6
doi: 10.1088/1748-0221/8/03/C03021
- 4) M. Aiello et al, A Dose Determination Procedure by PET Monitoring in Proton Therapy
IEEE Transactions on Nuclear Science, Volume: 60, Issue: 5, Part: 1, (2013) 3298-3304
Digital Object Identifier : 10.1109/TNS.2013.2266734
- 5) G. Sportelli et al., First full-beam PET acquisitions in proton therapy with a modular dual-head dedicated system.
Phys. Med. Biol. 59 (2014) 43–60
doi:10.1088/0031-9155/59/1/43
- 6) N. Camarlinghi et al., An In-beam PET System For Monitoring Ion-beam Therapy: Test On Phantoms Using Clinical 62 MeV Protons,
Journal of Instrumentation 9 C04005 (2014) 1-12
doi: 10.1088/1748-0221/9/04/C04005
- 7) A.C. Kraan et al., Proton range monitoring with in-beam PET: Monte Carlo activity predictions and comparison with cyclotron data
Physica Medica -European Journal of Medical Physics: 30 (2014) 559-569
doi:10.1016/j.ejmp.2014.04.003
- 8) A.C. Kraan et al., First tests for an on line treatment monitoring system with in-beam PET for proton therapy
Journal of Instrumentation, **10**, C01010 (2015) 1-11
doi:10.1088/1748-0221/10/01/C0101
- 9) A.C. Kraan et al., Online monitoring for proton therapy: a real-time procedure using a planar PET system
Nucl Instr Meth, **A786**, (2015), 120-126
DOI: 10.1016/j.nima.2015.03.059
- 10) V.Rosso et al., In-treatment tests for monitoring of proton and carbon-ion therapy with a large area PET system at CNAO
Nucl Instr Meth, **A824**, (2016), 228-232
DOI: 10.1016/j.nima.2015.11.017
- 11) E. Fabbiani et al., Performance Evaluation of a LYSO-based PET scanner for monitoring of dose delivery in hadrontherapy
Journal of Instrumentation, **10**, C12029 (2015) 1-11
doi:10.1088/1748-0221/10/12/C12029
- 12) G. Sportelli, N. Belcari, N. Camarlinghi, M.Ciocca, F. Collini, S. Molinelli,, M. Pullia, E. Zaccaro,. Del Guerra, V. Rosso
In-beam PET data characterization with the large area DoPET prototype
Journal of Instrumentation, **11**, C02089 (2016) 1-8
doi:10.1088/1748-0221/11/02/C02089
- 13) V. Rosso et al., DoPET: an in-treatment monitoring system for proton therapy at 62MeV
Journal of Instrumentation, **11**, C12029 (2016), 1-8
doi:10.1088/1748-0221/11/12/C12029

CONFERENZE

D1)N. Camarlinghi; G. Sportelli; G. Battistoni; N. Belcari; M. Cecchetti; G.A.P. Cirrone; G. Cuttone; S. Ferretti; A. Kraan; A. Retico; F. Romano; P.Sala; K.Straub; A. Tramontana; A. Del Guerra; V. Rosso

An In-beam PET System For Monitoring Ion-beam Therapy: Test On Phantoms Using Clinical 62 MeV Protons

Presented at **15th** International Workshop on Radiation Imaging Detectors, Paris (France),23-27 June 2013

D2)A.C. Kraan, G. Battistoni, N. Belcari, N. Camarlinghi, G.A.P. Cirrone, G. Cuttone, S. Ferretti, F. Romano, P. Sala, G. Sportelli, K. Straub, A. Tramontana, A. Del Guerra, V. Rosso.

Proton range monitoring with in-beam PET: Monte Carlo activity predictions and comparison with CATANA data

Presented at **1th** Particle Radiosurgery, A new Frontier in Physics in Medicine, University of Innsbruck in Obergurgl, Austria, August 25-29 2013

D3)V.Rosso

PET-in-beam: una tecnica per il monitoraggio dei trattamenti oncologici con ioni

XCIX Congresso Nazionale Societa' Italiana di Fisica, Trieste 23 - 27 settembre 2013

D4)S. Ferretti, G. Battistoni, N. Belcari, N. Camarlinghi, G.A.P. Cirrone, G. Cuttone, A. Ferrari, A.C. Kraan, F. Romano, P. Sala, G. Sportelli, K. Straub, A. Tramontana, A. Del Guerra, V. Rosso

PET monitoring in proton therapy: comparison between CATANA data and Monte Carlo simulations.

8° Congresso Nazionale AIFM, Torino 16-19 novembre, 2013

D5)A.C. Kraan, G. Battistoni, N. Belcari, N. Camarlinghi, F. Cappucci, M.Ciocca, A. Mairani, S. Molinelli, M. Pullia, A. Ferrari, S. Ferretti, P. Sala, G. Sportelli, A. Del Guerra, V. Rosso

Treatment monitoring with in-beam PET at CNAO: can in-spill data contribute?

Presented at **16th** International Workshop on Radiation Imaging Detectors, Trieste (Italy),22-26 June 2014

D6)N. Camarlinghi, A.C. Kraan, G. Battistoni, N. Belcari, F. Cappucci, M.Ciocca, A. Ferrari, S. Ferretti, A. Mairani, S. Molinelli, M. Pullia, A. Retico, P. Sala, G. Sportelli, A. Del Guerra, V. Rosso

Un tomografo a emissione di positroni per il monitoraggio della radioterapia con ioni: esperimenti su fantocci presso la linea di fascio del CNAO

100° Congresso Nazionale Societa' Italiana di Fisica, Pisa 22-26 Settembre 2014

D7) A.C. Kraan, G. Battistoni, N. Belcari, N. Camarlinghi, F. Cappucci, M.Ciocca, A. Mairani, S. Molinelli, M. Pullia, A. Ferrari, S. Ferretti, A. Retico, P. Sala, G. Sportelli, A. Del Guerra, V. Rosso

First tests for real-time treatment monitoring with a compact planar PET system at CNAO

Workshop on Range Assessment and Dose Verification in Particle Therapy, 29-30 /9, Dresden, Germany

D8) N. Camarlinghi, A.C. Kraan, G. Battistoni, N. Belcari, F. Cappucci, M.Ciocca, A. Ferrari, S. Ferretti, A. Mairani, S. Molinelli, M. Pullia, A. Retico, P. Sala, G. Sportelli, A. Del Guerra, V. Rosso

A compact In-Beam PET prototype for treatment monitoring: first tests at CNAO

2014 IEEE Nuclear Science Symposium and Medical Imaging Conference, 8-15 November, Seattle, Washington, USA

D9)V.Rosso, G. Battistoni, N. Belcari, N. Camarlinghi, M.Ciocca, F. Collini, A. Ferrari, S. Ferretti, A.C. Kraan, S. Lucenò, A. Mairani, S. Molinelli, M. Pullia, P. Sala, G. Sportelli, E. Zaccaro, A. Del Guerra

First tests for in-beam carbon therapy treatment monitoring with a planar PET system at CNAO

13th Pisa Meeting on Advanced Detectors, May 25-31, 2003 - La Biodola, Isola d'Elba, Italy

D10) F. Collini, G. Battistoni, N. Belcari, N. Camarlinghi, M.Ciocca, A. Ferrari, S. Ferretti, A.C. Kraan, S. Lucenò, S. Molinelli, M. Pullia, P. Sala, G. Sportelli, E. Zaccaro, A. Del Guerra, V. Rosso

Test preliminari per il monitoraggio in-beam di trattamenti con fasci di protoni e ioni carbonio con un sistema PET planare al CNAO

101° Congresso Nazionale Societa' Italiana di Fisica, Roma 21-25 settembre 2015

D11)V. Rosso, G. Battistoni, N. Belcari, N. Camarlinghi, G.A.P.Cirrone, F. Collini, G. Cuttone, M.Ciocca, A. Del Guerra, A. Ferrari, S. Ferretti, A.C. Kraan, A. Mairani, M. Pullia, S. Molinelli, F. Romano, P. Sala, G. Sportelli, E. Zaccaro

DoPET: an in-treatment monitoring system for particle therapy, ICTR-PHE 2016, Ginevra 15-19 febbraio 2016

D12) V. Rosso: On-line monitoring for particle beams

The 3rd ELIMED Workshop: Medical and multidisciplinary applications of laser-driven ion beams at ELI-Beamlines. Laboratori Nazionali del Sud of INFN, Catania 7-10 September 2016

D13)L. Brombal, N. Belcari, M.G. Bisogni, L. Cristoforetti, N. Camarlinghi, A. Del Guerra, F. Fracchiolla, R. Longo, M. Morrocchi, R. Righetto, V. Rosso, M. Schwarz, G. Sportelli

Prime valutazioni delle capacità di risposta del sistema DoPET nel monitoraggio dei trattamenti presso il centro di protonterapia di Trento

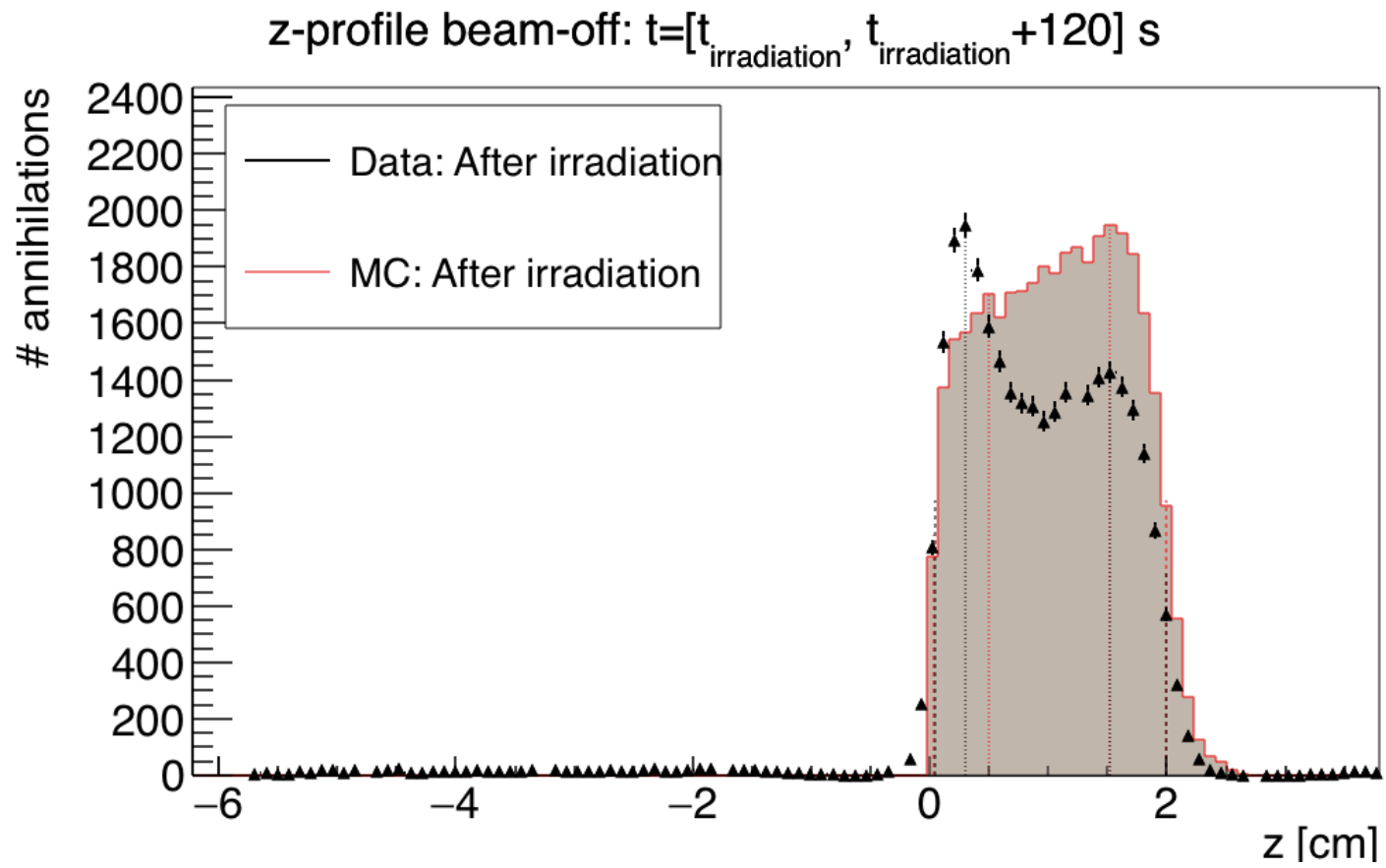
XVII Convegno Nazionale SIRR, Trento, 25-27 September 2016

Con 10^9 protoni:

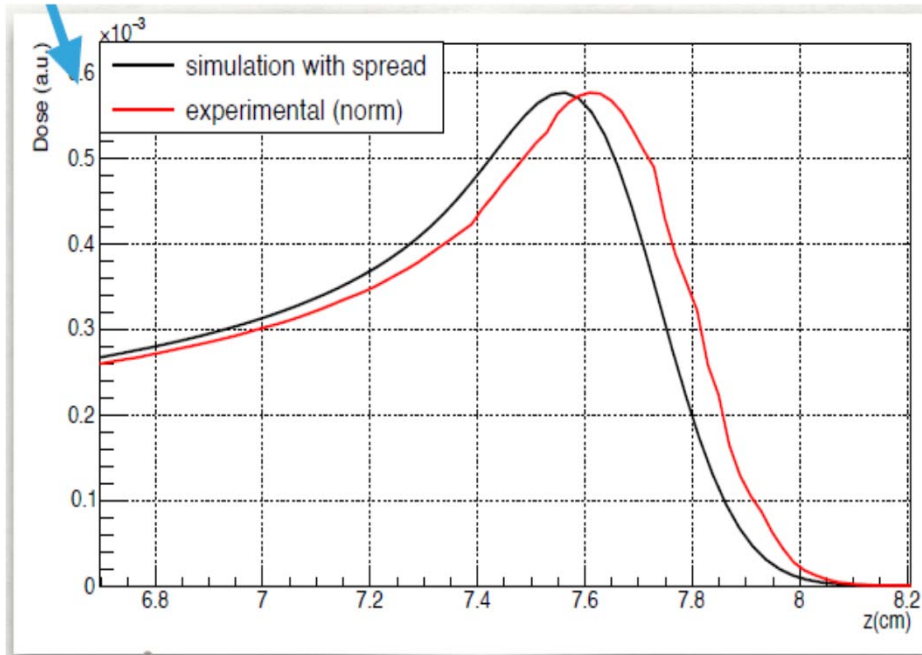
- Non tutti i file con 10^9 sono stati ancora analizzati.
- Passando a 10^9 protoni l'errore aumenta

contributi	11-C (%)	15-O (%)	10-C (%)	8-B (%)
PMMA-BRAIN 10^{10}	46.9 ± 0.3	43.6 ± 0.4	8.8 ± 0.2	0.68 ± 0.24
PMMA- BRAIN 10^9	47.5 ± 1.6	42.1 ± 1.8	9.6 ± 0.6	0.74 ± 0.10

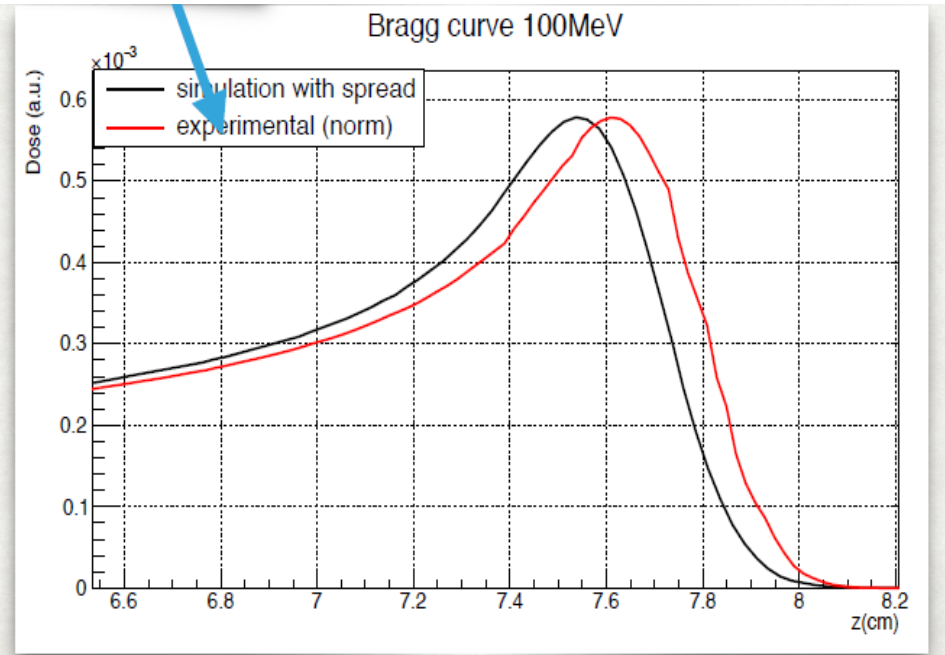
PROBLEMATICHE



I=78 eV



I=76.9 eV



100MeV	sperimentale	sim. I=78eV	sim. I=76.9eV
peak (mm)	76.09	75.63	75.38
R50 (mm)	78.29	77.63	77.38

