PET imaging for proton therapy: analysis of in-beam time profiles

Aafke Kraan, INFN Pisa

On behalf of the DOPET and INSIDE experiments

Outline

- **Introduction to proton therapy**
- **Positron Emission Tomography (PET)**
- **DoPET detector & simulation**
- **Results**
- **Outlook**
- **Conclusions**

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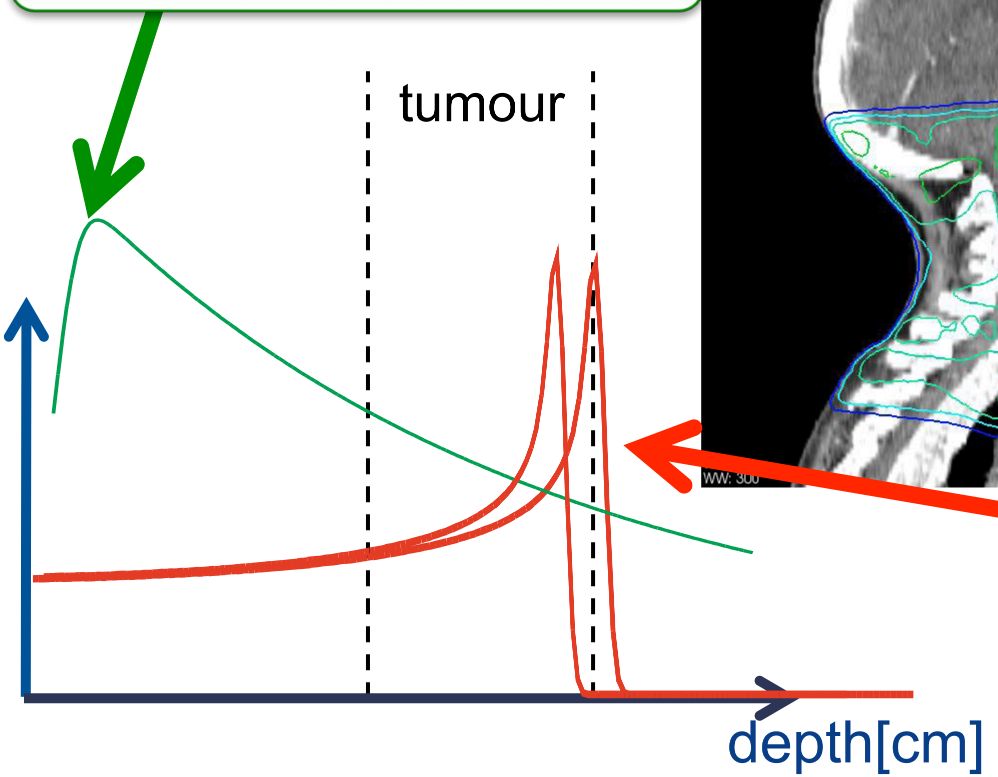
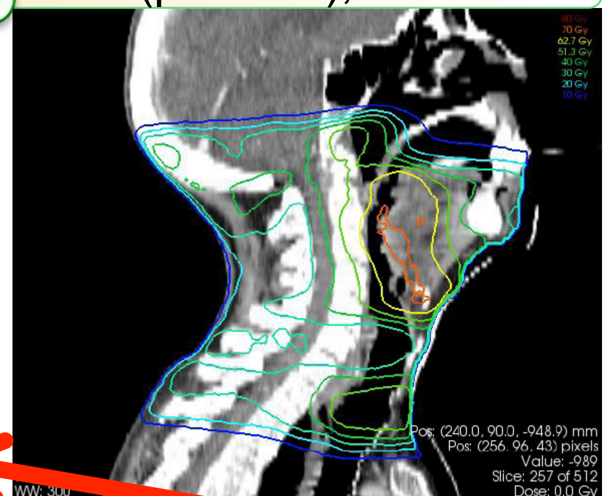
Introduction

Charged particles have highly advantageous dose profile compared to photons!

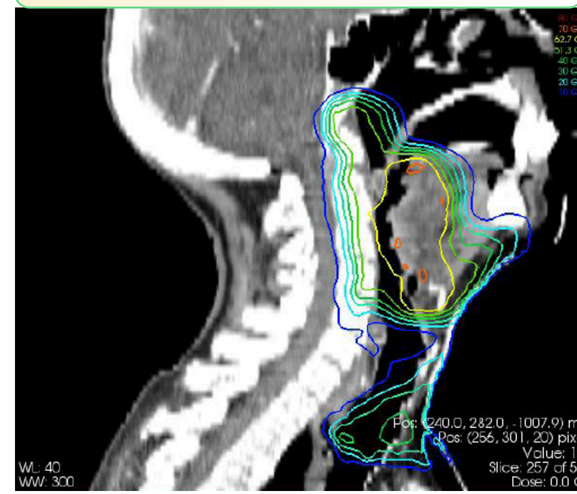
Photons: high dose delivered in front and behind tumor



IMRT (photons), 10 directions



IMPT (protons), 3 directions



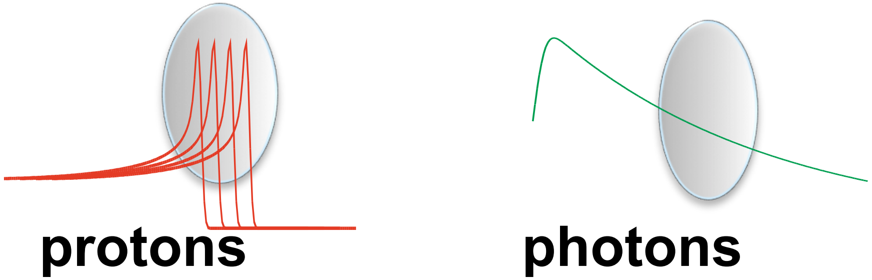
Protons: Bragg Peak: Dose spot

- Energy ~ depth
- Nr. protons ~ height

Introduction

One of the main disadvantages of charged particle therapy is the sensitivity to uncertainties:

- Steep dose gradients
- Matching of many individual pencil-beams



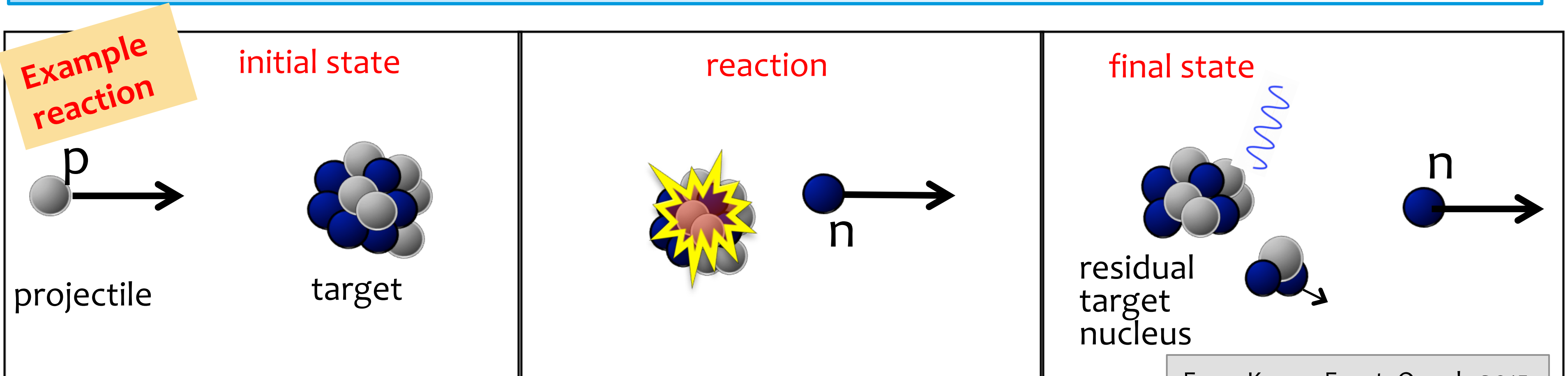
- **Anatomical changes:** (internal organ motion, changes in air cavities, tumour regression, weight loss
- **Proton range** (calibration CT apparatus, proton stopping power, implants)
- **Patient inter-fractional setup** (daily positioning on the couch)

If we miss the target (for whatever reason) we can cause a damage… (much more serious than for photons)

It would be good, if we could monitor the range of the protons!

Introduction

What happens in the human body when a proton of energy range 50-250 MeV hits the human body?



From Kraan, Front. Oncol., 2015

What kind of fragments?
- Many different types… …
- Most relevant here:
  β^+ **emitting nuclei like ^{15}O, ^{11}C, ^{10}C, etc.**

  → can be detected with a PET system

^{15}O, ^{15}N, ^{14}N, ^{13}C, ^{12}C, ^{11}C, ^{10}B, ^{8}Be, ^{6}Li, ^{4}Be, ^{4}He, ^{3}He, ^{3}H, ^{2}H, ^{1}H, …

See for instance: Tommasino & Durante, Cancers 2015,7

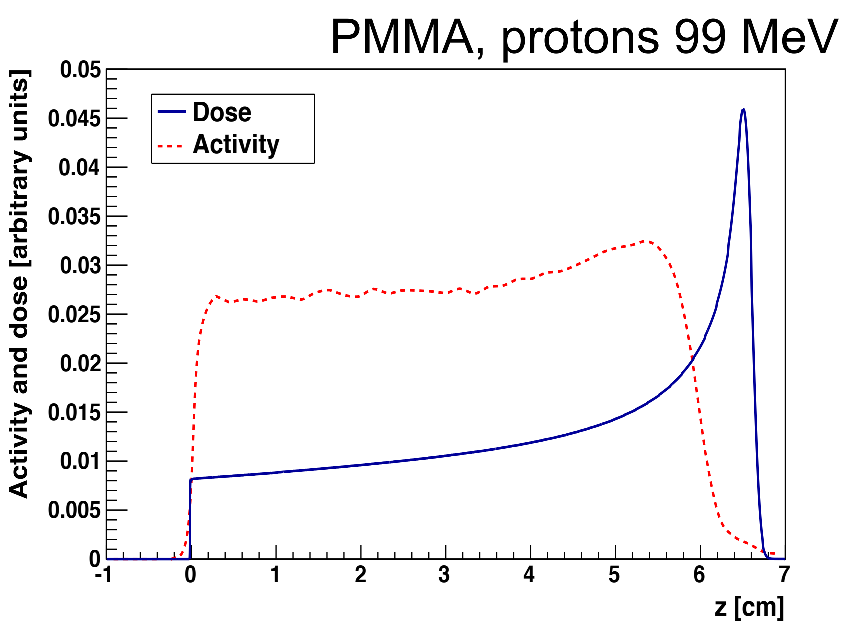
Positron Emission Tomography

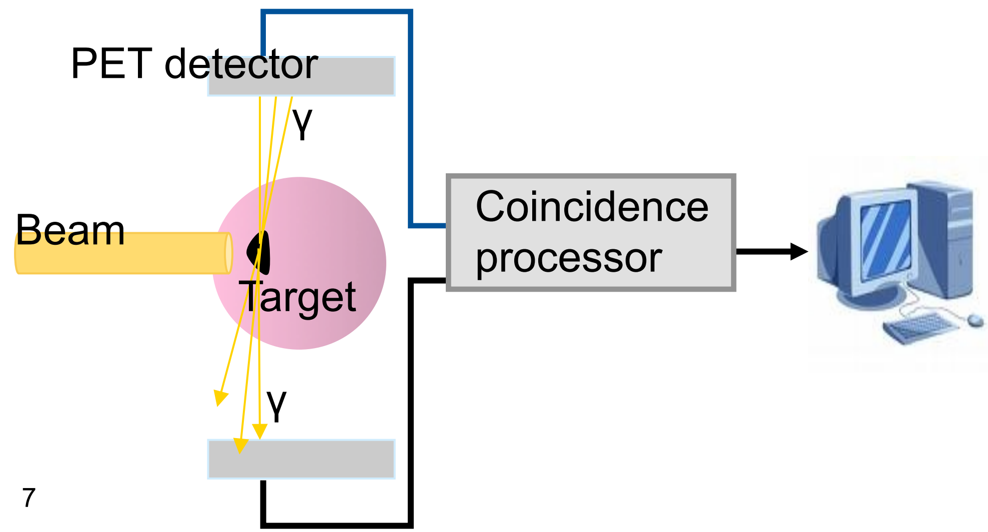
- β^+ emitters can be detected with PET (Positron-Emission-Tomography)

β^+ emitter	Half-life
^{11}C	20 min
^{15}O	2 min
^{13}N	10 min
^{10}C	19 s
…	

Method first explored by Enghardt, Parodi, Nishio, Iseki, Crespo, Fiedler, etc…

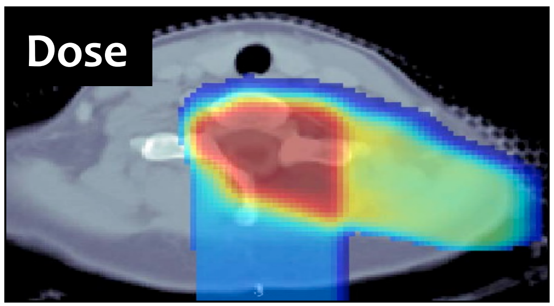
- PET β^+ activity is (indirectly) related to proton range and dose
- Can compare MC activity prediction with PET data (or data with data)

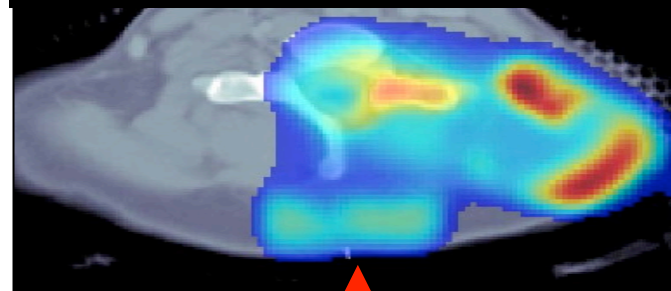




What's usually done

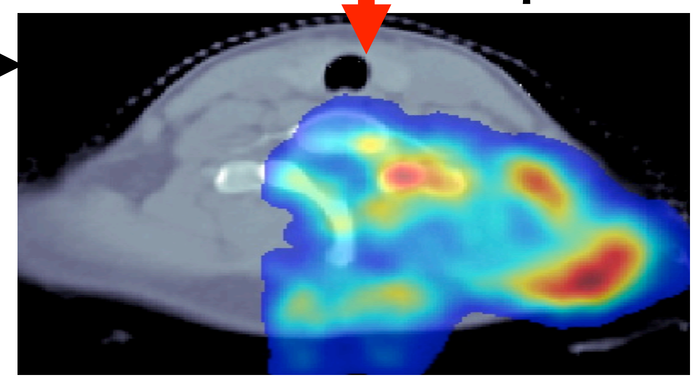
Dose prescription → Treatment plan → FLUKA calculation → Expected activity map (in some time-frame)





compare → action?

Measured activity map →



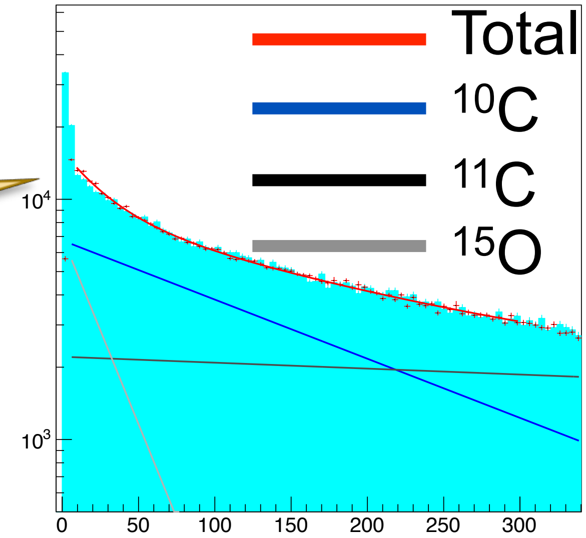
- FLUKA MC calculations to predict the PET activity
- Mostly done: compare **space** distributions

Parodi, IJROPB, 2007

Goal of this study

In addition to space distributions, study time distributions!

Shape of decay curve (nr decays/s) depends on the decaying isotopes and thus on the irradiated tissue



This presentation:

- Extract **fractions of ^{15}O, ^{11}C and ^{10}C in phantoms in in-beam PET data**
- Can PET decay-rates give an indication about elements in the phantom?
- Possibly useful for:
  - **Validation of the nuclear physics models in FLUKA**
  - To investigate biological washout models + perfusion in patients
  - To calculate the elemental composition of the irradiated tissue (detect changes of oxygenation in tumors?)

- Few words about **INSIDE** project

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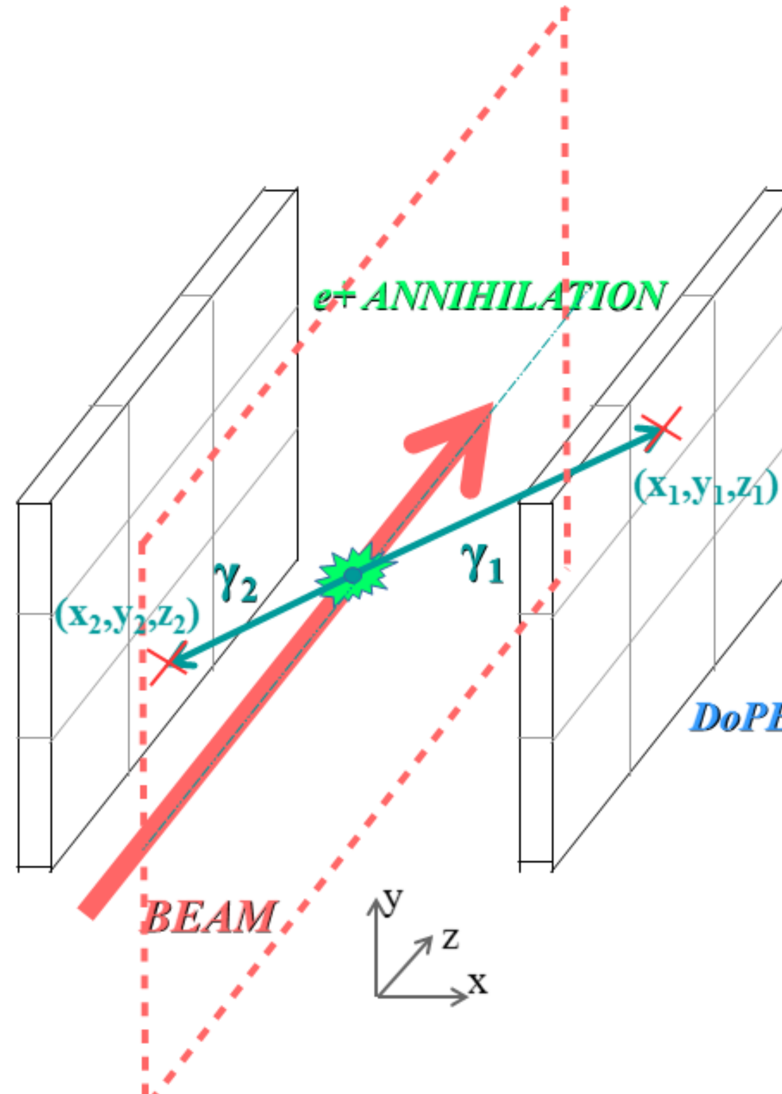
PET system

PET system

- ✓ Two heads, 38 cm apart
- ✓ Each plane 16 x 16 cm^2
- ✓ Each head contains 9 modules
- ✓ LYSO crystal scintillator
- ✓ Position sensitive photomultipliers
- ✓ Dedicated fast front-end electronics
- ✓ DAQ system, 5 ns coincidence window
- ✓ Reconstruction algorithm: MLEM

See for instance:
Sportelli G, et al. Phys Med Biol (2014) 59(1):43–60. doi: 10.1088/0031-9155/59/1/43
V.Rosso et al, JINST 12, 2017



Data acquisition

Phantoms

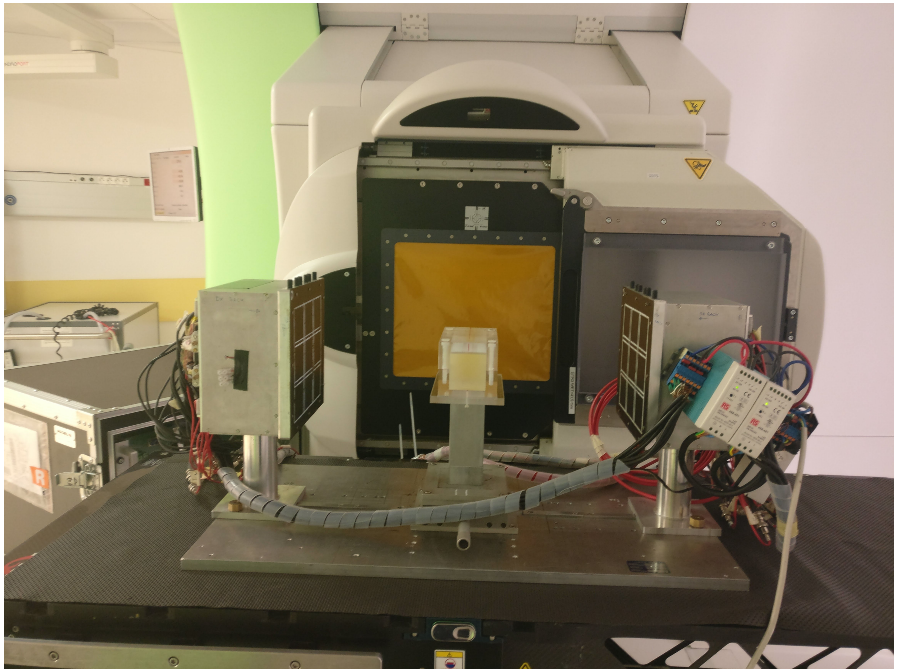
- ✓ **Phantoms:** PMMA, PE and Water.

Irradiations:

- ✓ Phantoms were irradiated for 5 s with single pencil beams (10^{10} protons, FWHM=10.7 mm) at the **Cyclotron Centre of the Bronowice** proton therapy centre in Krakow, Poland.
- ✓ 130 MeV protons

Acquisitions:

- ✓ 5 minutes after data taking



FLUKA Simulation & analysis

Simulation

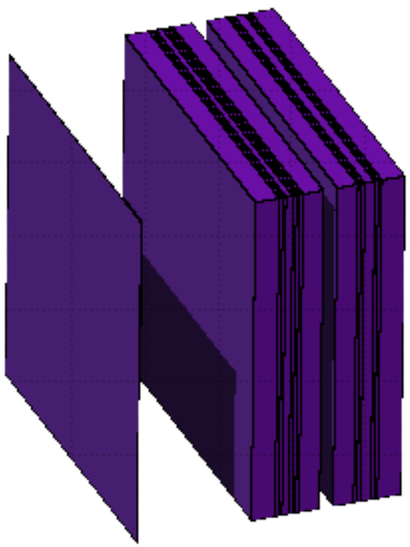
- ✓ Used **FLUKA** to simulate all data acquisitions and PET system

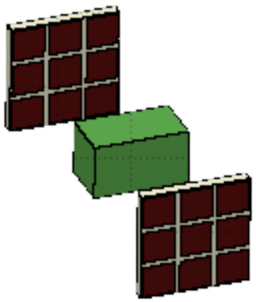
Thesis by A. Topi, 2018

- ✓ Mgdraw.f written to score position and times of beta+ decays
- ✓ Detector hits & time stored
- ✓ In-house reconstruction

S. Muraro, NIMA936, 2019

- ✓ Beam-delivery simulated





Analysis:

- ✓ The activity distributions in **space** → shape and absolute height of 1-D z-profiles (beam-axis).
- ✓ The activity distributions in time, i.e., **the decay rates** → exponential fit to estimate the contribution of ^{15}O ($t_{1/2}$=2 min), ^{11}C ($t_{1/2}$=20 min) and ^{10}C ($t_{1/2}$=19 s) in the phantoms

→ **Compare data with MC**

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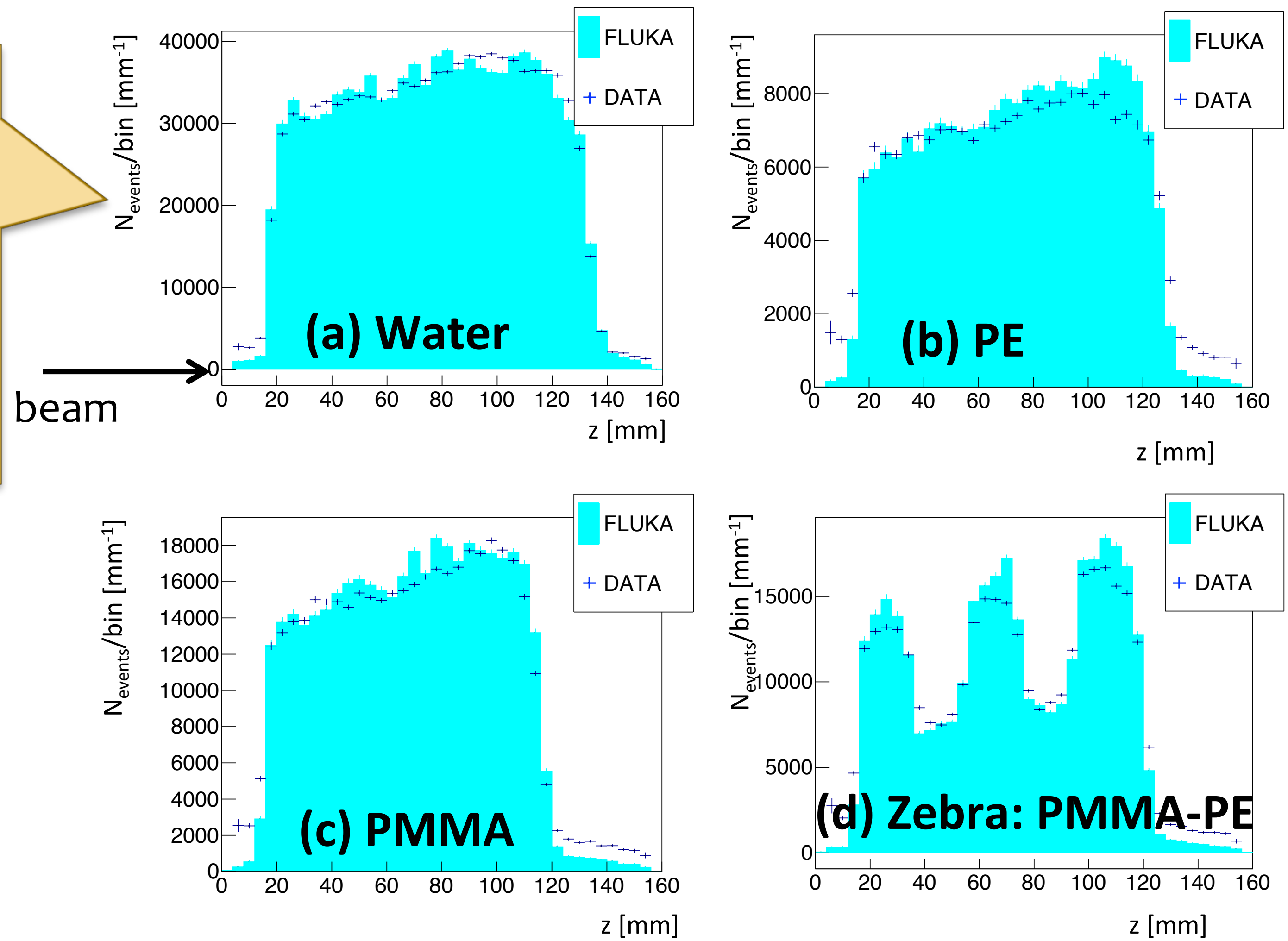
Results

1-D activity distribution along the beam-axis: FLUKA and data, for 130 MeV protons on a different targets

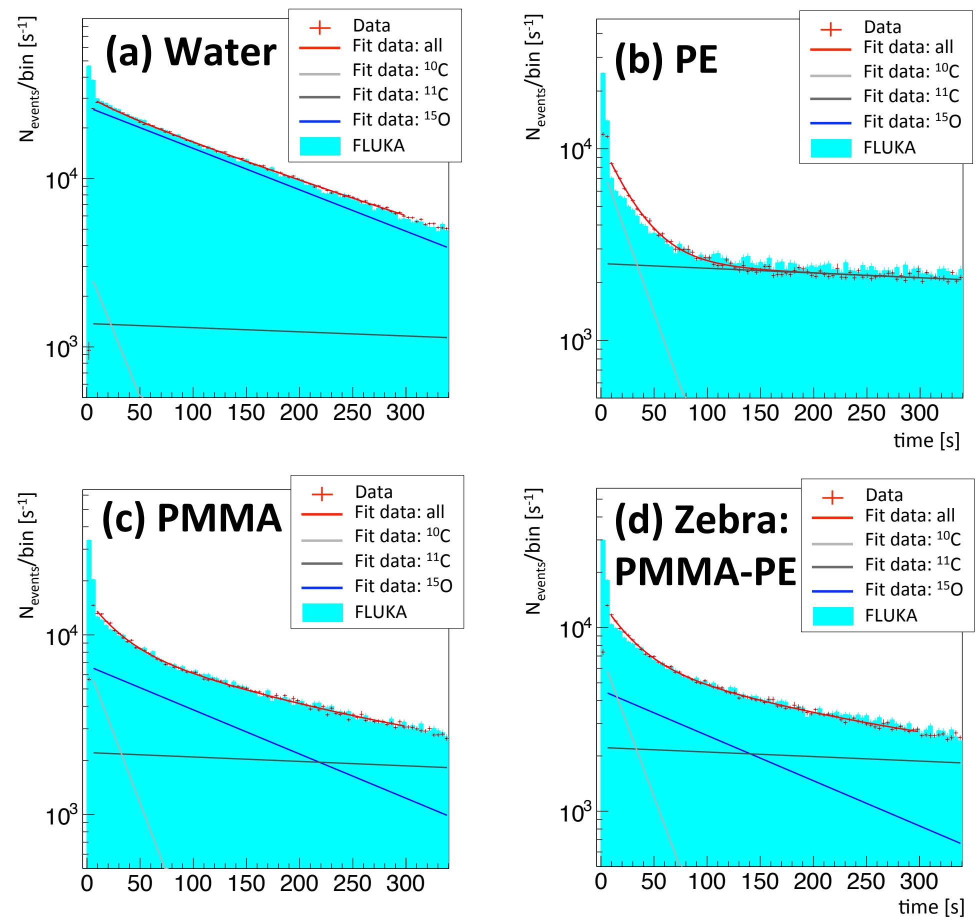


A good agreement between FLUKA and data is seen!.

Results

1-D decay rate for 4 different phantoms fitted with the contributions from ^{15}O, ^{11}C, and ^{10}C

Kraan, et al, JINST 14, 2019



Observations

- PE, PMMA and Zebra: at small times: data is somewhat higher than FLUKA...
- A good agreement between FLUKA and data is seen!.

Results

Fitted values were used to calculate the relative fractions of ^{15}O, ^{11}C, and ^{10}C in the time interval from 8 to 300 s.

β+ emitter	Water		PE		PMMA		Zebra	
	DATA	MC	DATA	MC	DATA	MC	DATA	MC
^{15}O	89.4%	91.5 %	0 %	0%	55.5 %	58.5 %	45.4 %	45.7 %
^{11}C	9.1%	6.2 %	79.3 %	85.7 %	35.7 %	34.9 %	43.5 %	46.2 %
^{10}C	1.6%	2.4 %	20.7 %	14.3 %	8.8 %	6.6 %	11.1 %	8.1 %

- Overall agreement good!
- ^{10}C is somewhat higher in data than in MC

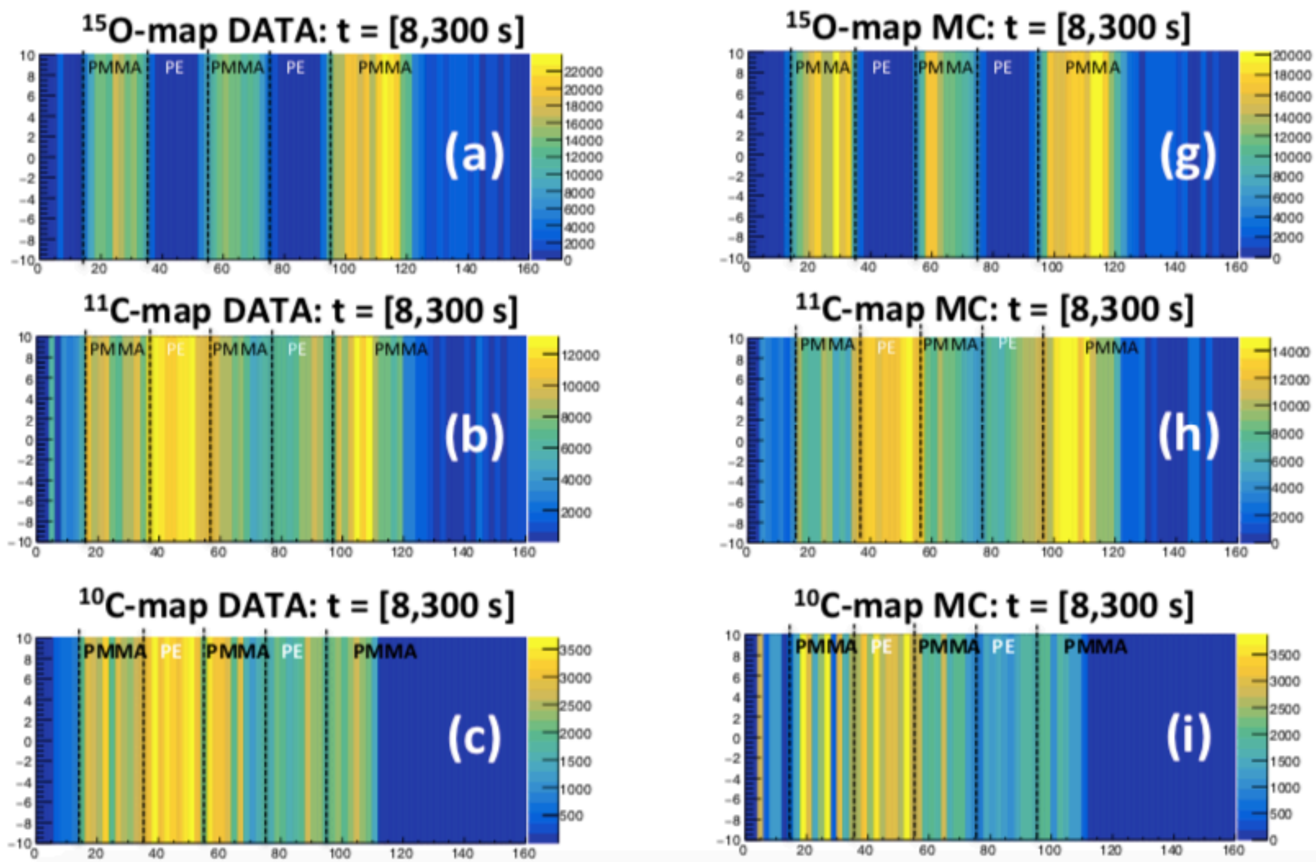
Seen also for instance in P. Cambraia Lopes, J. Bauer, A. Salomon, et. al., First in situ TOF-PET study using digital photon counters for proton range verification, Phys. Med. Biol. 61 (2016) 6203

More data needed!

Results

By dividing the phantom into different slices (2 mm in z, 20 mm in x and y) and repeating the fit in each slice, it is possible to approximately map the amount of ^{15}O, ^{11}C and ^{10}C. In Fig. 5 we show a 1-D map for ^{15}O for the Zebra phantom data.

From the time fit: number of β^+ decays per slice from ^{15}O, ^{11}C, ^{10}C as a function of z in a time-interval from 8 to 300 s, for the Zebra phantom.



INSIDE

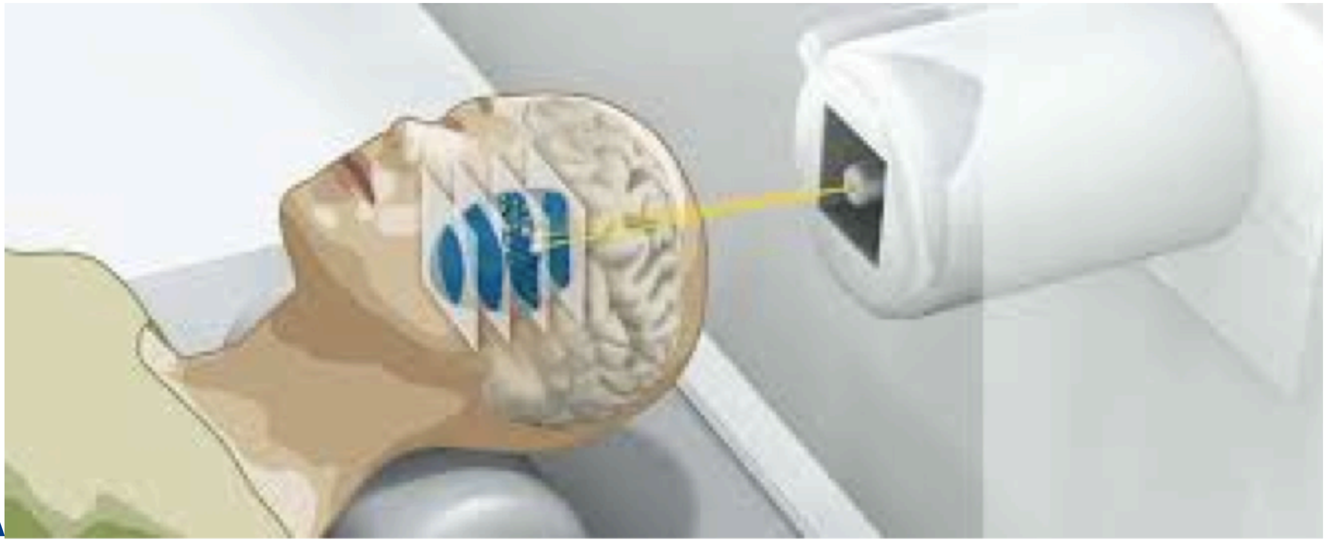
INnovative **S**olutions for **I**n-beam **D**osim**E**try in Hadrontherapy

- In-beam PET detector installed at CNAO (Centro Nazionale di Adroterapia Oncologica)
- Online-PET (during treatment) in between the spills of the synchroton
- Simulation framework with FLUKA

F. Pennazio, E. Fiorina, V. Ferrero, et al

- First clinical test @CNAO, 1-2 Dec. 2016
- **Bi-modal:** apart from PET, also charged particle detector!

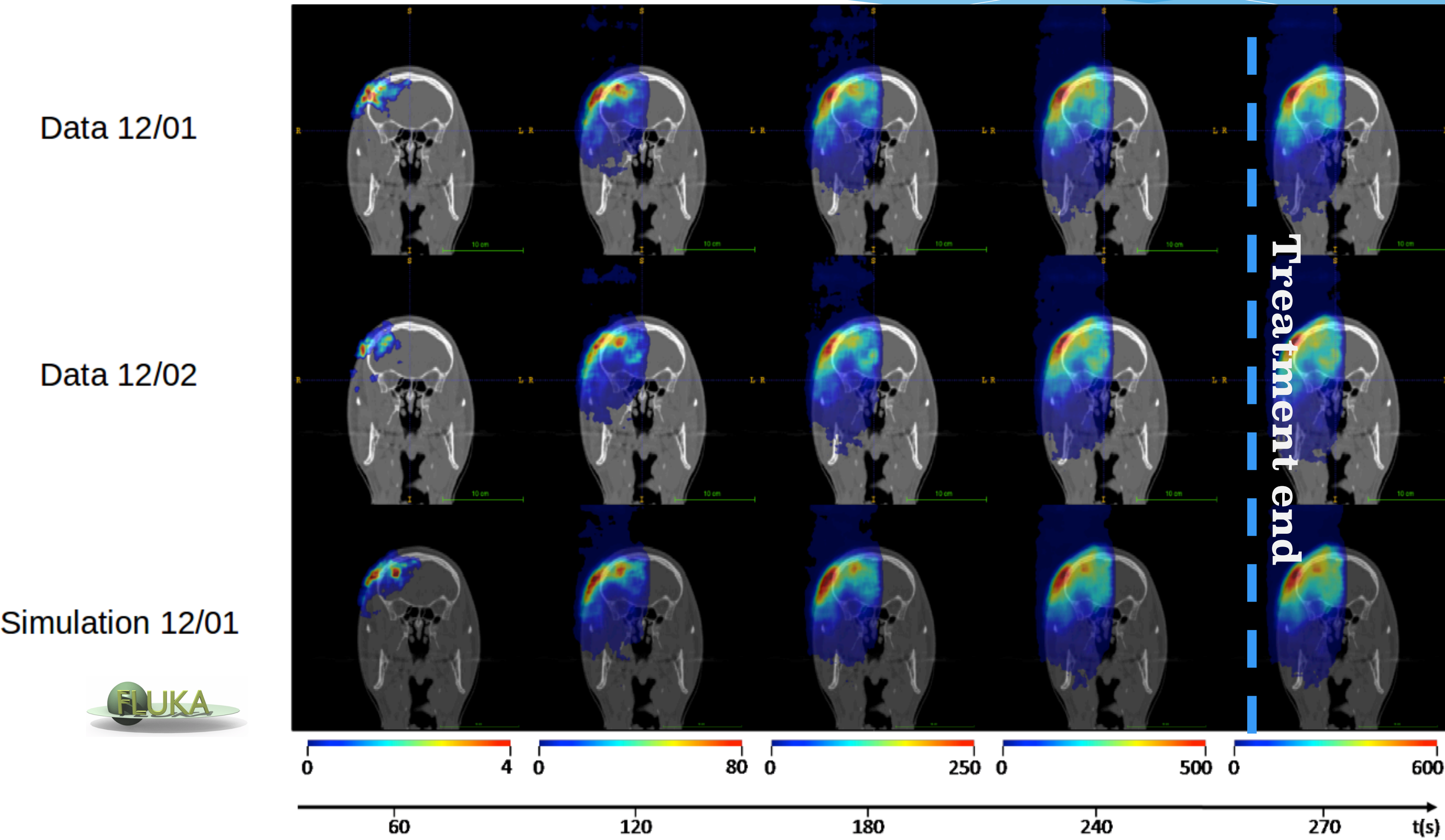
See G. Bisogni et. al., J.Medical Imaging 01005, 2017



InSide

INSIDE

INSIDE



Elisa Fiorina et al., INFN Torino and CNAO, Physica Medica 51 2018

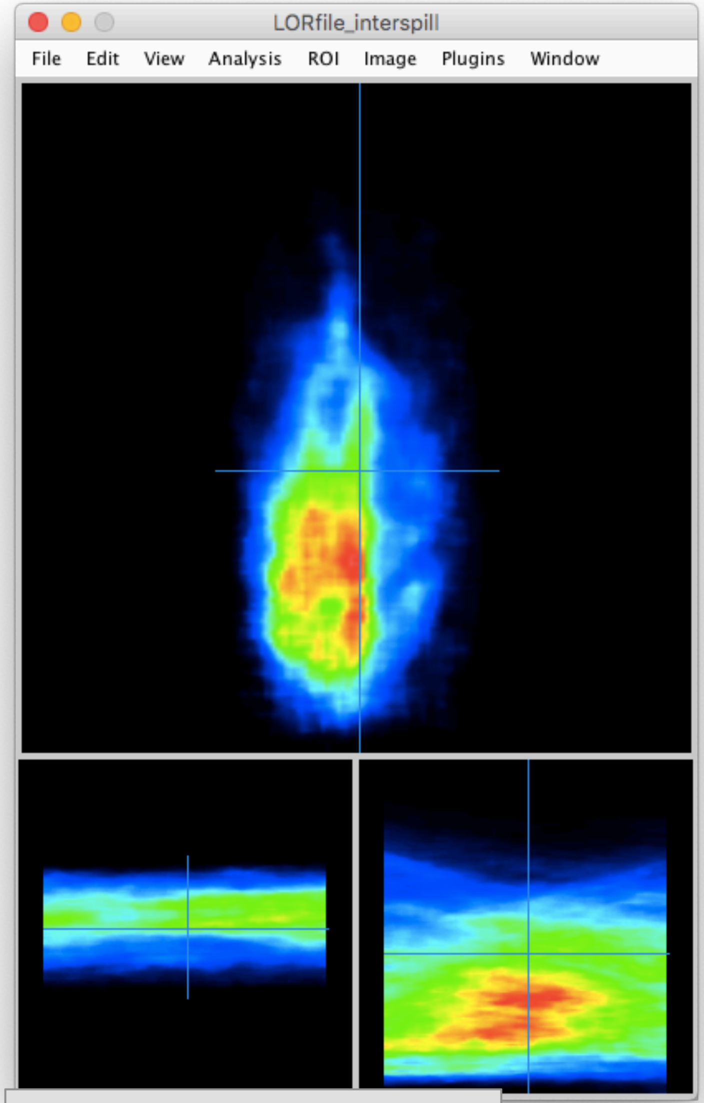
Simulation challenges

Large number of protons has to be simulated

For 1 liter tumor 2 Gy (RBE): > 10^{11} protons needed…

In practise, simulate a fraction of the plan

Setting up simulation framework to be able to quickly simulate patient treatments (Torino, Pisa)



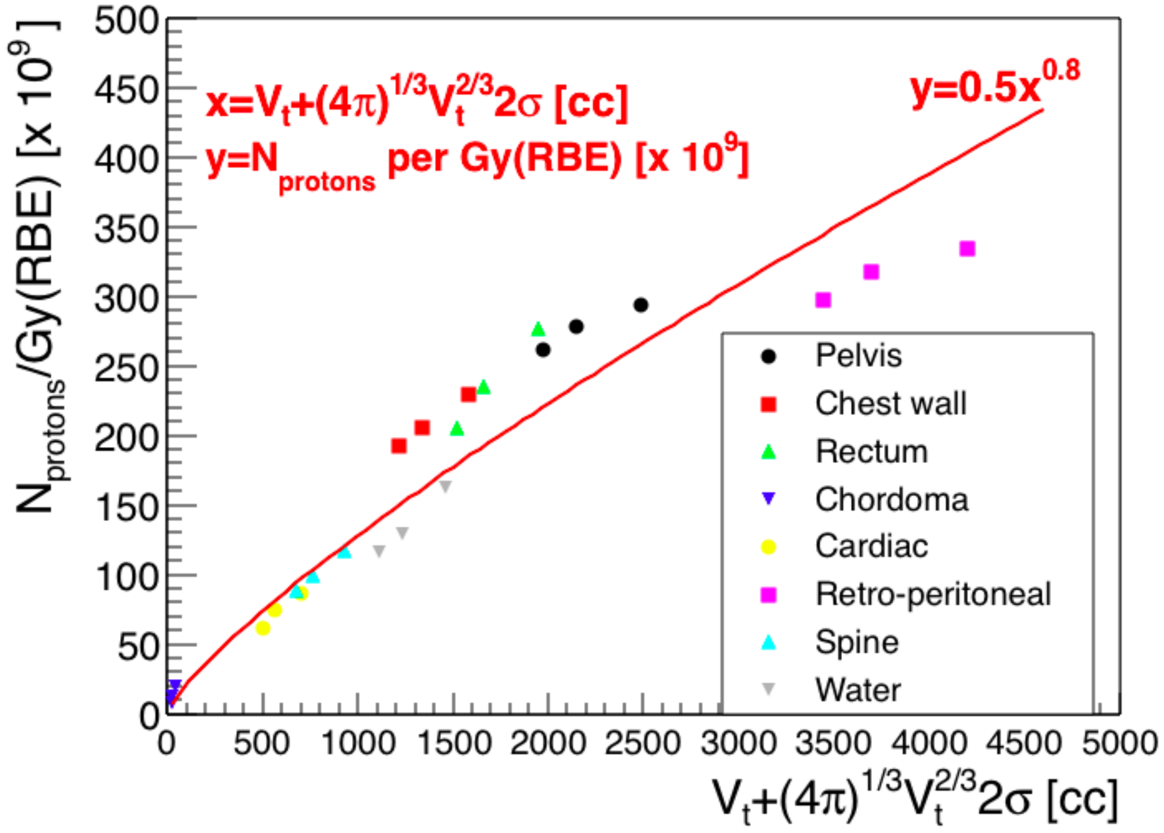
A. Berti (master student Pisa)

Conclusions

- **Fractions of the various PET isotopes could be accurately monitored in space and time.**
- Extracted fractions of ^{15}O, ^{11}C and ^{10}C for various phantoms in time intervals immediately after irradiation until 5 minutes after irradiation.
- Based on 10^{10} protons, i.e., only a small fraction of what's typically delivered in an entire treatment (~10^{11} protons/Gy/liter).
- With a simple voxel-by-voxel fit-approach the contributions of the various isotopes could be localized.
- Example of simple experimental setup, useful for validation of FLUKA hadronic models
- New studies to be done with DoPET at CATANA
- **INSIDE:** clinical trial ongoing to evaluate the use of online-PET →lot's of data to be analyzed

Thanks for your attention

Nr protons vs tumor volume



$$N_{protons}\ per\ Gy(RBE)[\times 10^9] \simeq 0.5[V_t + (4\pi)^{\frac{1}{3}} V_t^{\frac{2}{3}} 2\sigma]^{0.8}$$