ONLINE RANGE MONITORING IN HADRONTHERAPY WITH THE INSIDE PET SCANNER

PhD: Veronica Ferrero Tutor: Dr. Piergiorgio Cerello XXXI PhD cycle







HADRONTHERAPY

"Radiation therapy is the medical use of ionizing radiation to treat cancer. When the irradiating beams are made of charged particles (protons and other ions, such as carbon), radiation therapy is called Hadrontherapy."

The European Network for LIGht ion Hadron Therapy



CNAQ

CNAO - TERA Foundation, Pavia
Synchrotron
60-250 MeV/u protons
120-400 MeV/u carbon ions
Protons since 2011
Carbon ions since 2012

CORRIERE DELLA SERA / SPORTELLO CANCRO

NUOVILEA

Adroterapia rimborsata dal Servizio Sanitario contro 10 tipi di tumori

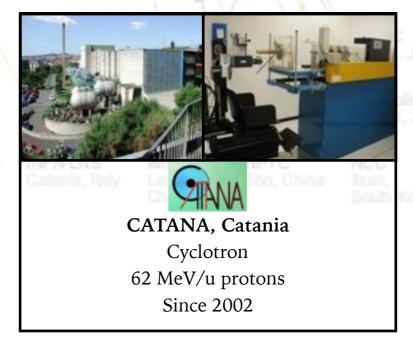
Pubblicato in Gazzetta Ufficiale il decreto ministeriale sui nuovi Livelli Essenziali d'Assistenza: l'adroterapia, cura i per i tumori resistenti alla radioterapia tradizionale e non operabili, rimborsata in tutte le Regioni

18th March 2017

~ 80 operating centers in the world 41 new centers in the next 2 years



Since 2014



TREATMENT ACCURACY ASSESSMENT

BETHE-BLOCH EQUATION

$$-\frac{dE}{dx} = Kz^2 \frac{Z}{A} \frac{1}{\beta^2} \left[\ln \frac{2m_e c^2 \beta^2 \gamma^2 T_{max}}{I^2} - \beta^2 - \frac{\delta \left(\beta \gamma\right)}{2} \right]$$

 $K = 4\pi N_A r_e^2 m_e c^2$

Z Atomic number of absorber

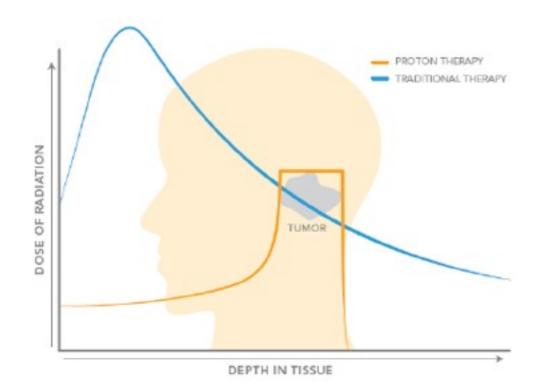
A Atomic mass of absorber

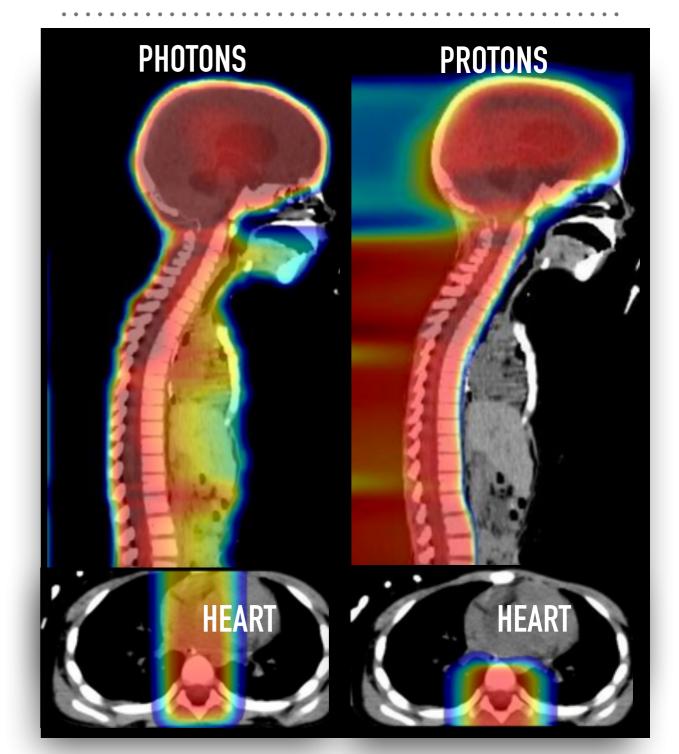
 m_e Mass of an electron

 r_e Classical radius of an electron

I Mean excitation energy

 T_{max} Maximum Kinetic energy which can be imparted to a free electron in one collision





Mirabell R et al., Potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of pediatric tumor, Int. Jour. Rad. Onc. Phys. 2002, 54 (3) 824

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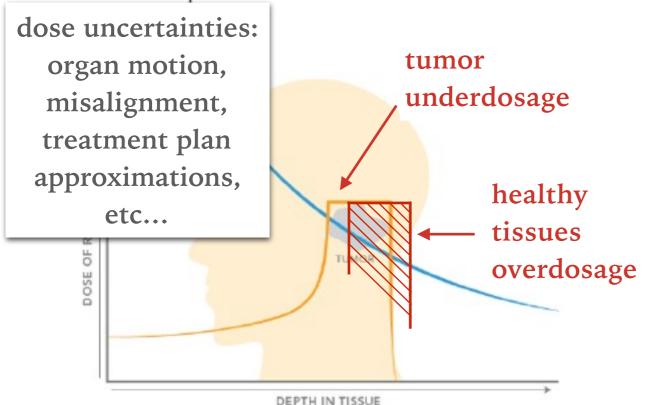
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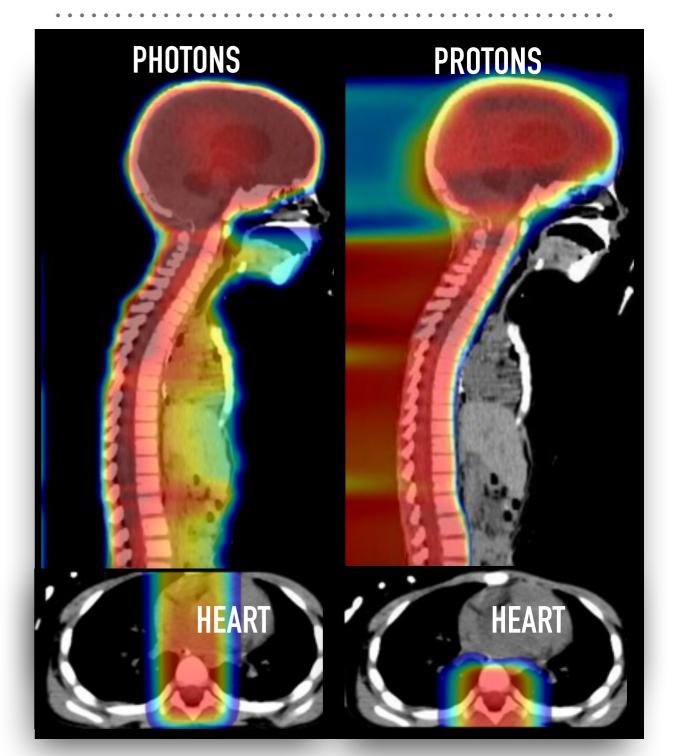
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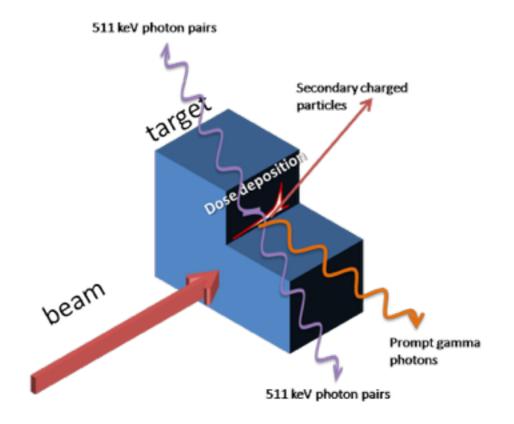
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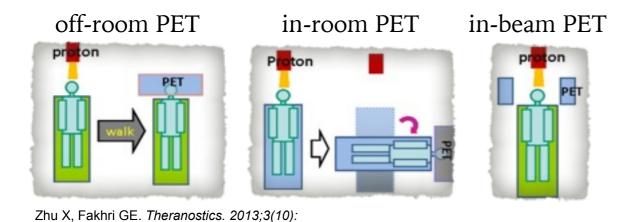




Mirabell R et al., Potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of pediatric tumor, Int. Jour. Rad. Onc. Phys. 2002, 54 (3) 824

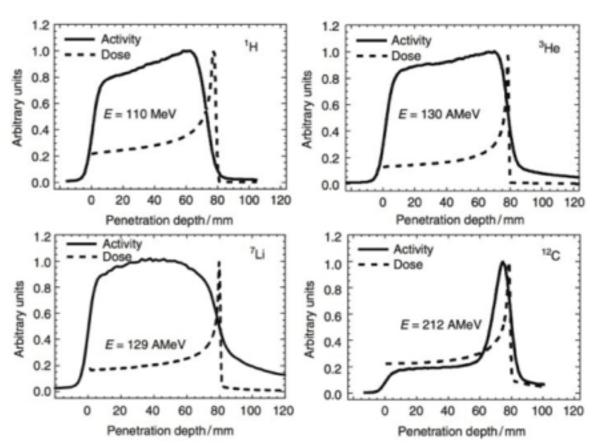
PARTICLE RANGE VERIFICATION





Target	β^+ isotopes	Half-life
С	¹⁰ C, ¹¹ C	19.29 s, 20.33 m
N	^{13}N	9.96 m
O	¹⁴ O, ¹⁵ O	70.61 s, 122.24 s
P	^{30}P	2.50 m
Ca	³⁸ K	7.64 m

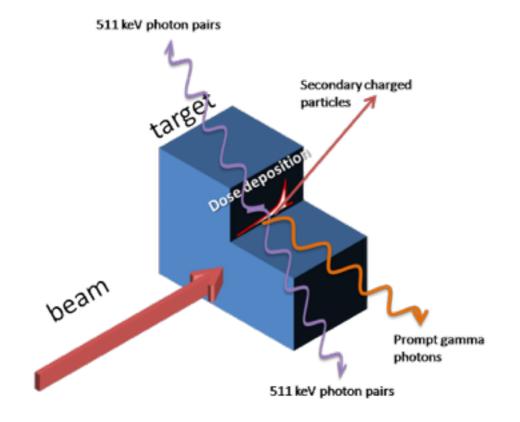
E Palomares et al. Study of the reliability of the cross sections used to model the production of PET isotopes with proton beams. *Phys. Med. Biol. 2011; 56:2687-98*



Fiedler F., et al. Online irradiation control by means of PET. *Ion Beam Therapy Fundamentals, Technology, Clinical Applications.* Berlin: Springer-Verlag (2012) p. 527-43

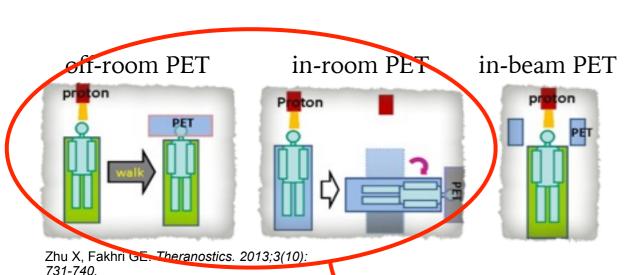
731-740.

PARTICLE RANGE VERIFICATION

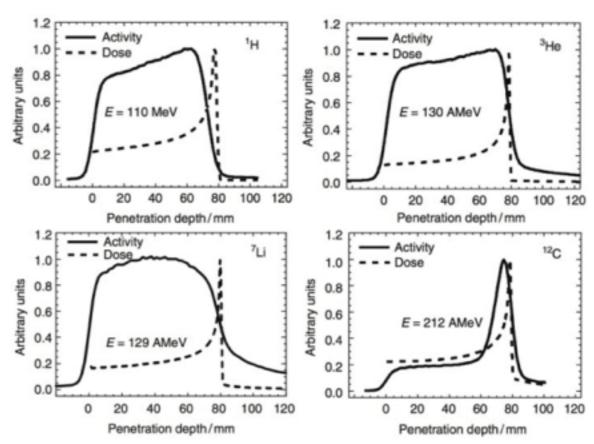


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loss of signal due to short half lives, higher washout



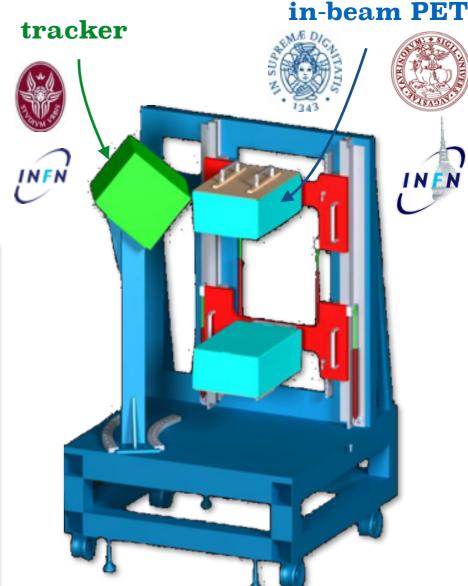
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The Inside Project @ CNAO

INnovative Solutions for In-beam DosimEtry in Hadrontherapy



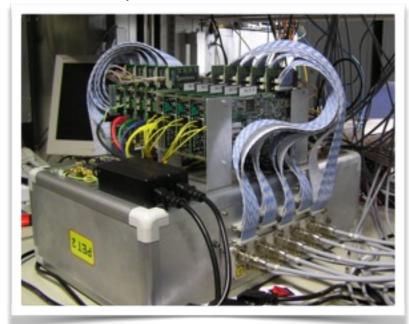
National Center of Oncological Hadrontherapy (CNAO), Pavia, Italy



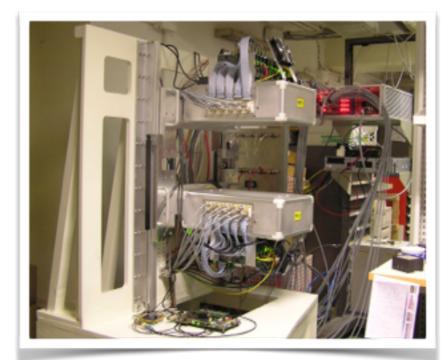
- Bimodal system (tracker under characterization, PET installed at CNAO)
- Integrated in the treatment room
- Provides a feedback during the treatment

THE INSIDE IN-BEAM PET

January 2016, INFN Torino



PET heads assembled and tested



Completed PET detector (running)

March 2016, CNAO, Pavia



November 2017, INFN Torino

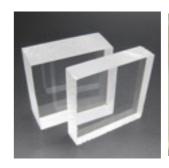


CHARACTERIZATION TESTS











FDG, ⁶⁸Ge rods

PMMA, anthropomorphic phantom

First results of the INSIDE in-beam PET scanner for the on-line monitoring of particle therapy treatments

M.A. Piliero, a,b,1 N. Belcari, a,b M.G. Bisogni, a,b N. Camarlinghi, a,b P. Cerello, b,c S. Coli, d A. Del Guerra, a,b V. Ferrero, c,d E. Fiorina, c,d G. Giraudo, d E. Kostara, b M. Morrocchi, a,b F. Pennazio, c,d C. Peroni, c,d G. Pirrone, a,b A. Rivetti, d M.D. Rolo, d V. Rosso, a,b G. Sportelli, a,b R. Wheadon d

INSIDE in-beam positron emission tomography system for particle range monitoring in hadrontherapy

Maria Giuseppina Bisogni, a.b.* Andrea Attili, c.d Giuseppe Battistoni, a. Nicola Belcari, a.b. Niccolo Camarlinghi, a.b. Piergiorgio Cerello, a. Silvia Coli, a. Alberto Del Guerra, a.b. Altredo Ferrari, Veronica Ferrero, c.d. Elisa Florina, a. Giuseppe Giraudo, a. Eleftheria Kostara, a.b. Matteo Morrocchi, a.b. Francesco Pennazio, a. Cristiana Peroni, c.d. Maria Antonietta Piliero, a.b. Giovanni Pirrone, a.b. Angelo Rivetti, Manuel D. Rolo, a. Valeria Rosso, a.b. Paola Sala, Giancario Sportelli. A.b. and Richard Wheadon.

The INSIDE project: in-beam PET scanner system features and characterization

V. Ferrero on behalf of the INSIDE collaboration

The INSIDE project: on-line monitoring and simulation validation with the in-beam PET scanner

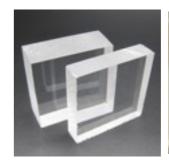
V Ferrero 1,2 on behalf of the INSIDE collaboration

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The INSIDE project: in-beam PET scanner system features and characterization IPRD, Siena (talk)

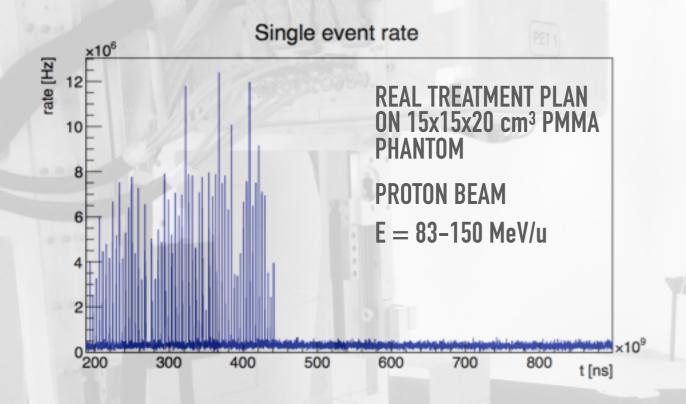
V. Ferrero on behalf of the INSIDE collaboration

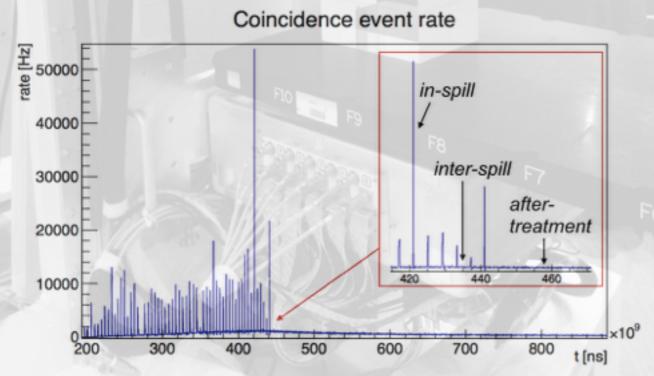
The INSIDE project: on-line monitoring and simulation validation with the in-beam PET scanner

V Ferrero 1,2 on behalf of the INSIDE collaboration

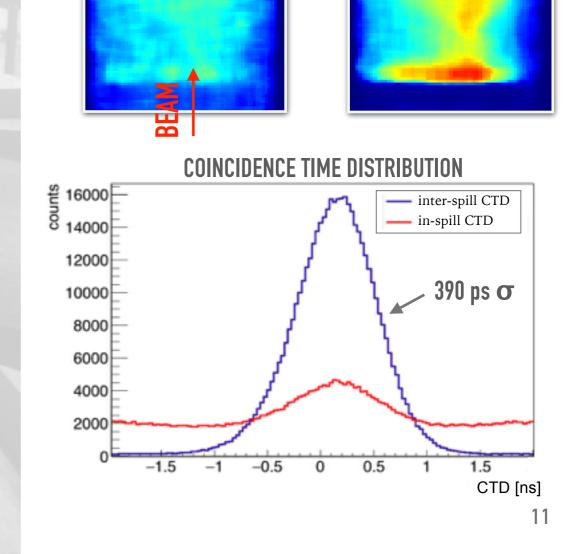
YRM, Torino (talk)

THE INSIDE PROJECT:IN-BEAM PET SCANNER SYSTEM FEATURES AND CHARACTERIZATION (14TH IPRD, SIENA)





vferrero@to.infn.it, INFN and University of Torino

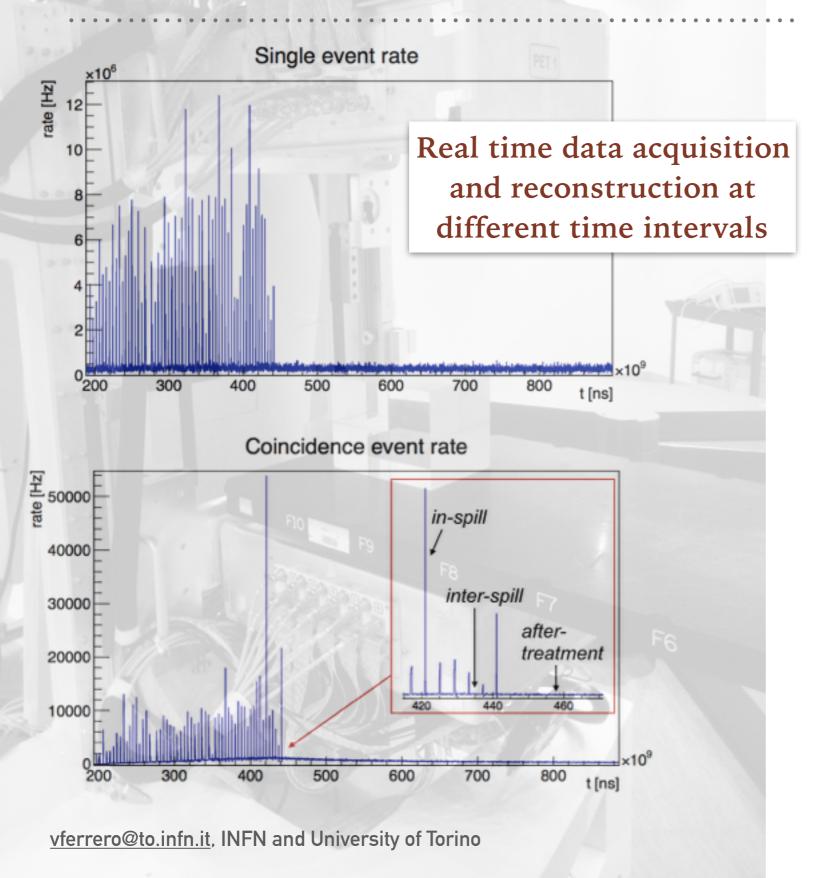


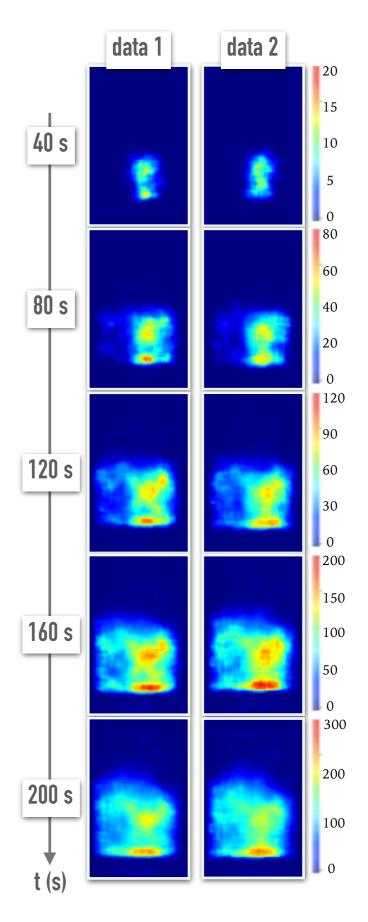
in-spill

inter-spill

THE INSIDE PROJECT:IN-BEAM PET SCANNER SYSTEM FEATURES AND

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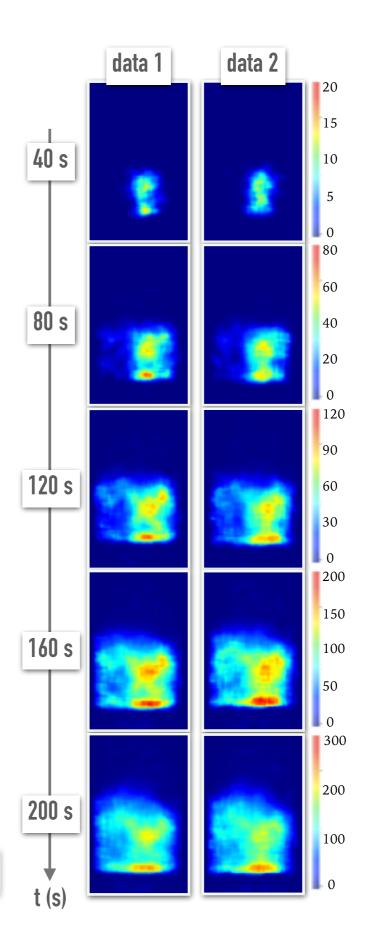




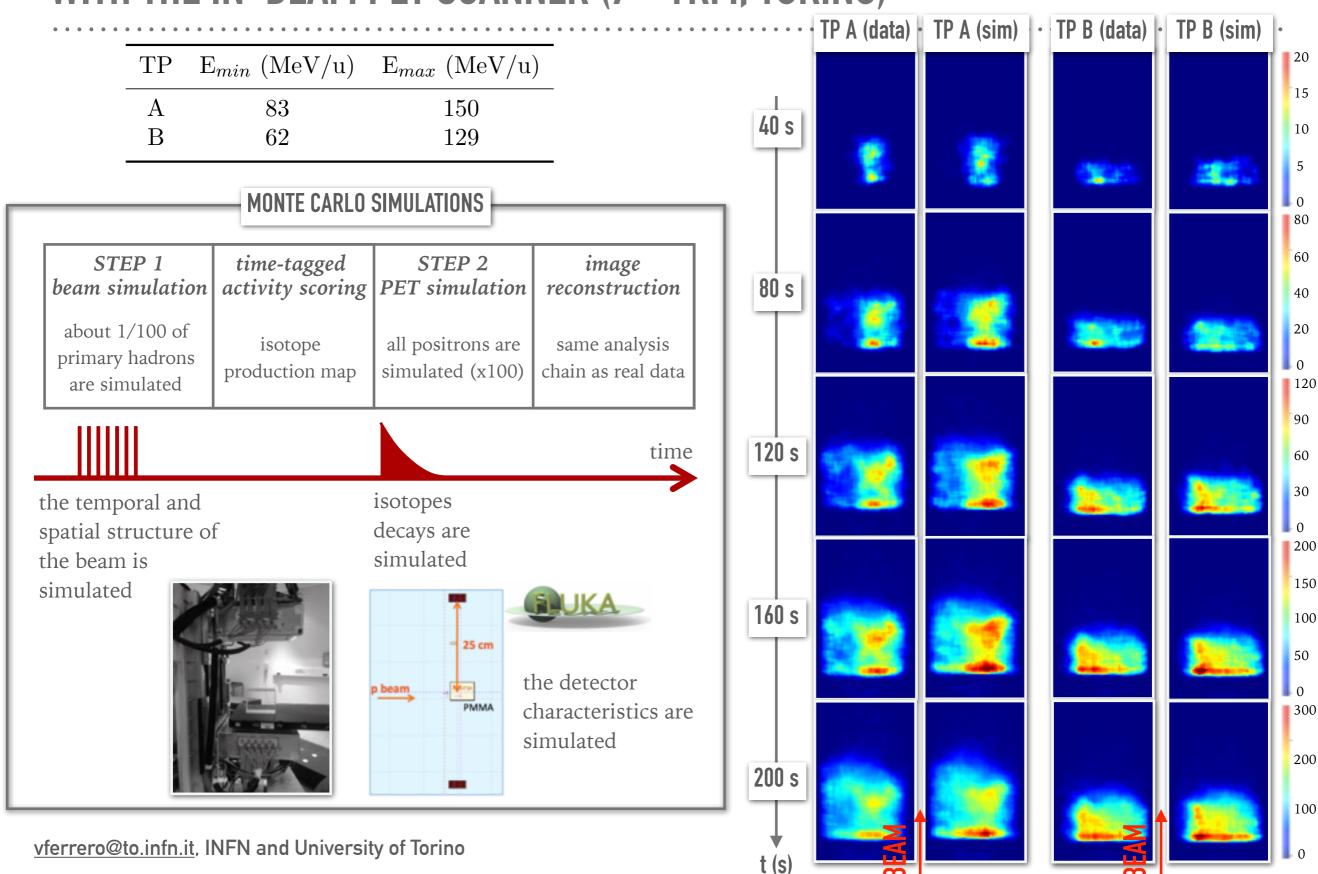
COINCIDENCES ANALYSIS

```
eronica@mag11xl:~$ INSIDEWriteLORfile
rogram to analise DAQ data and write LORfile for image reconstruction, usage:
-h [ --help ]
                                  Produce this help message
-D [ --DataType ] arg
                                  Data type permitted:
                                   'w' binary file 20 modules, Clock 120 MHz,
                                  beam test Feb 2016. Option -g needed for
                                  this data type.
                                   's' binary file 20 modules, Clock 120 MHz,
                                  beam test Apr 2017 in/interspill selected by
                                  server. NB if acquired data have a wrong
                                  threshold, use data type 'w' to better
                                  select in/interspill
-L [ --LORF1le(s) ] arg
                                  Input DAQ LORFile(s) (.bin)
-C [ --ChannelMap ] arg
                                  /ChannelMap.txt
-g [ --RootFile ] arg
                                  [DataType 'w'] GUI root file (forwarded
                                  data) needed for inspill/interspill
                                  selection (only for data type 'w')
-t [ --spillThreshold ] arg
                                  [optional!] Threshold (Hz) to discriminate
                                  in- and inter-spill data, default 450000 Hz
                                  (only for data type 'w')
                                  [optional!] Creates histogram.root file with
                                  DAQ data
-i [ --startTime ] arg
                                  [optional!] Cuts DAQ data from time
                                  startTime (s)
-e [ --endTime ] arg
                                  [optional!] Cuts DAQ data to time endTime
-j [ --nbinTime ] arg
                                  [optional!] Number of bins in the time
                                  histograms.
-w [ --coincWindow ] arg
                                  [optional!] Sets coincidence window
                                  (default: 2ns)
-r [ --EnergyWindow ] arg
                                  [optional!] Applies new energy window to
                                  data, /EnergyWindow.txt
-o [ --EnergyWindowOnBoard ] arg [optional!] Saves additional TOT shift in
                                  histogram.root, /EnergyWindowOnBoard.txt
```

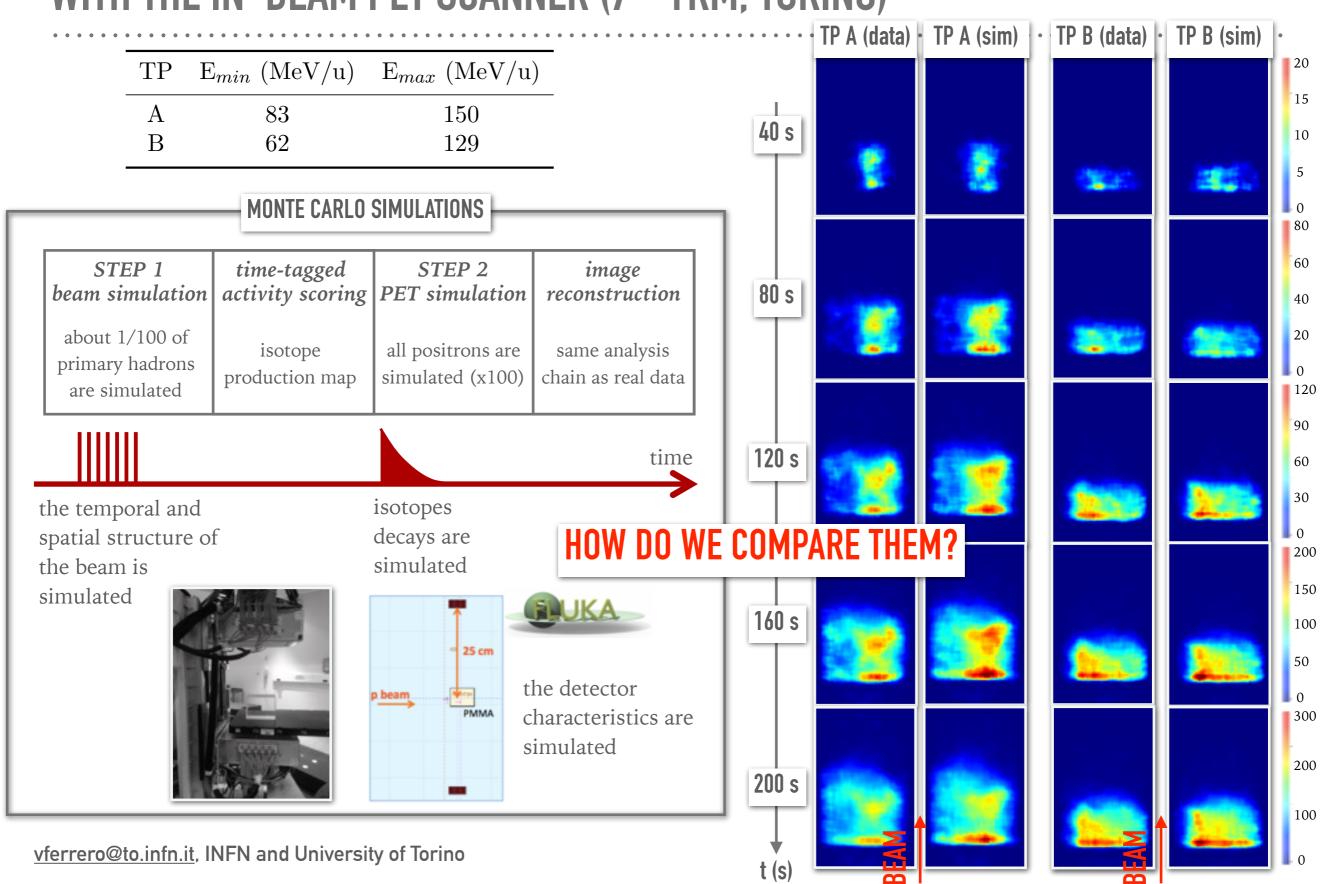
- ➤ Can be launched as soon as the server saves LOR files
- ➤ Finds and analyses coincidences over a certain time window
- Can apply time selection
- Produces a listmode coincidences file compatible with the reconstruction program
 C++. ROOT/BOOST LIBRARIES



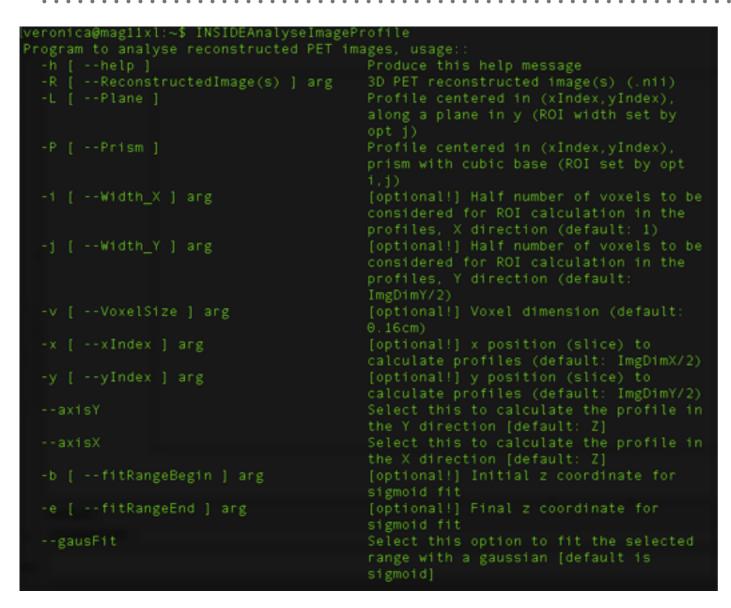
THE INSIDE PROJECT:ONLINE MONITORING AND SIMULATION VALIDATION WITH THE IN-BEAM PET SCANNER (7th YRM, TORINO)



THE INSIDE PROJECT:ONLINE MONITORING AND SIMULATION VALIDATION WITH THE IN-BEAM PET SCANNER (7th YRM, Torino)

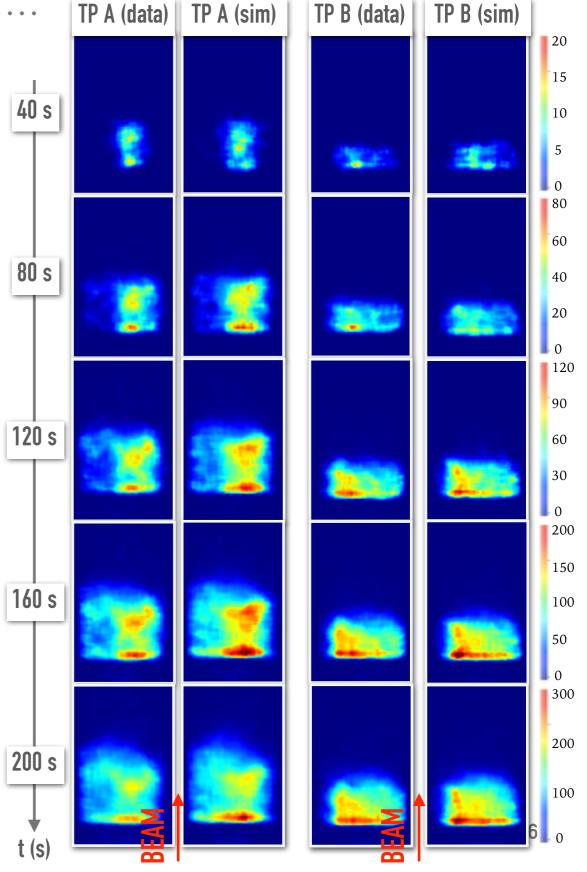


ACTIVITY PROFILE

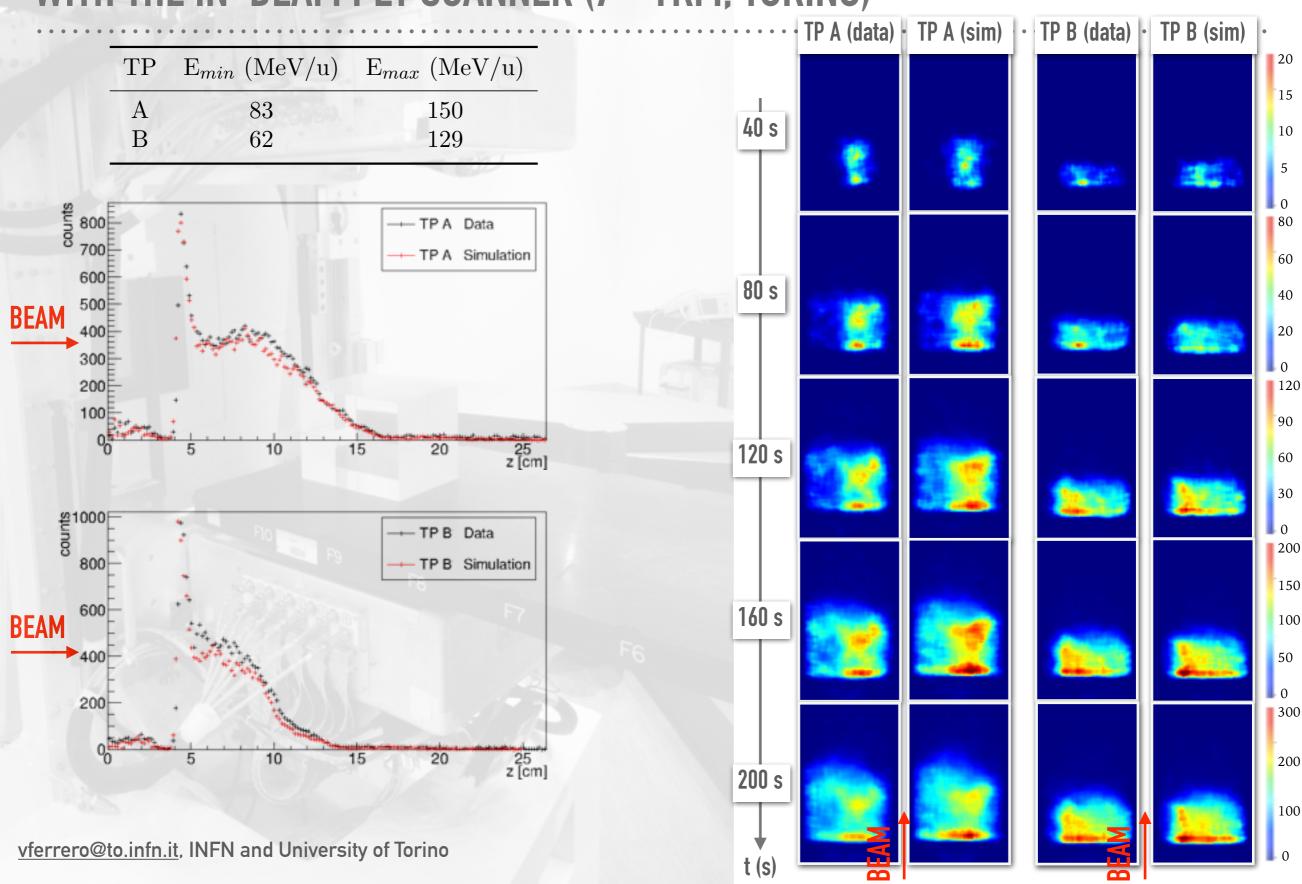


- Can compare several images
- ➤ Image profile on preferred direction in a selectable subimage
- ➤ Calculates range with sigmoid or gaussian function in the interval specified by the user

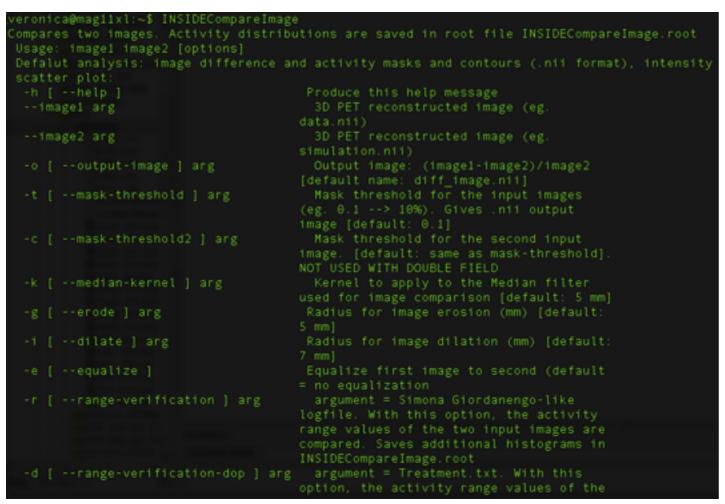
C++, ROOT/BOOST/ITK LIBRARIES



THE INSIDE PROJECT:ONLINE MONITORING AND SIMULATION VALIDATION WITH THE IN-BEAM PET SCANNER (7th YRM, Torino)

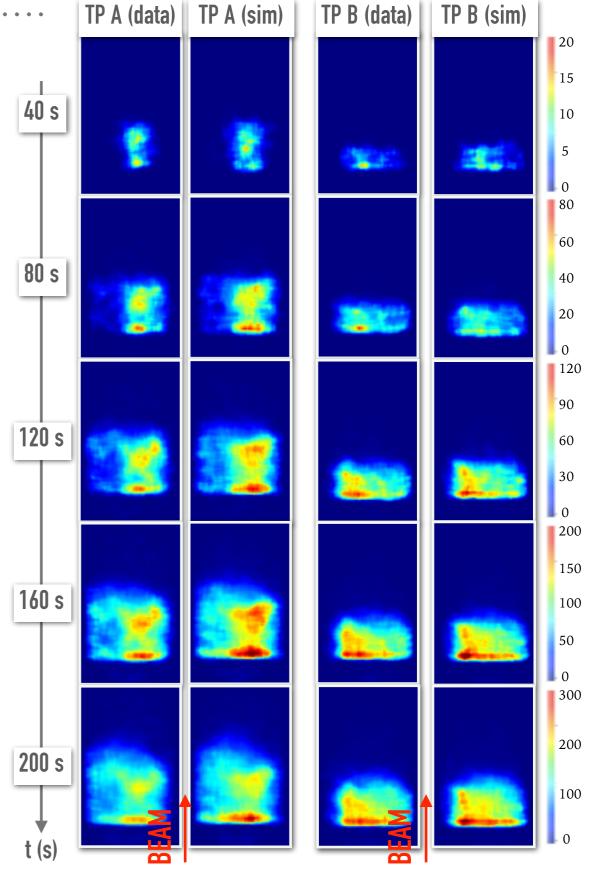


ACTIVITY COMPARISON

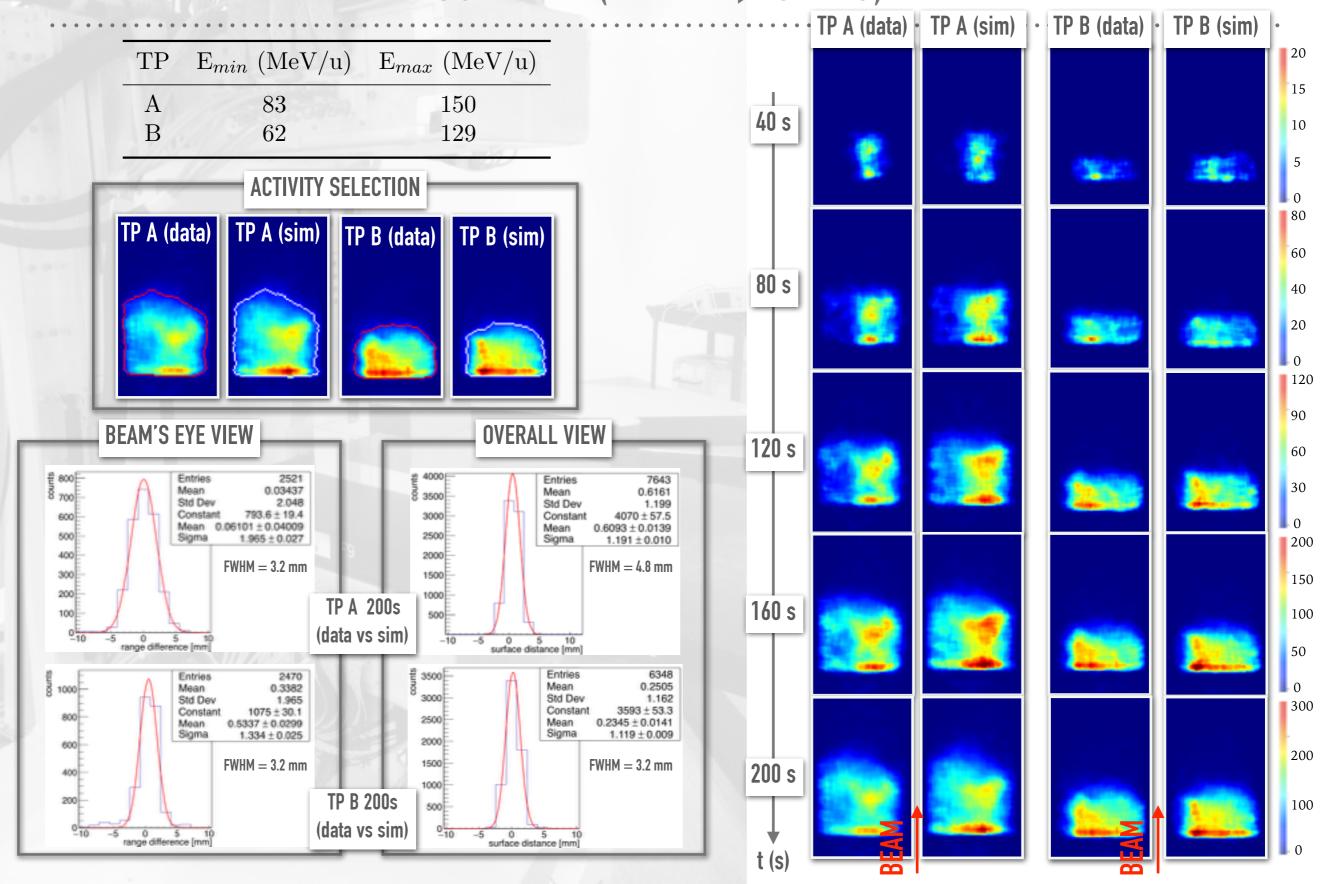


- Compares two images
- ➤ Can be launched in time (bash script)
- ➤ Selects the activity through the application of image filtering and compares the images 3-dimentionally
- Can use the treatment plan spatial information to select a sub-image of activity

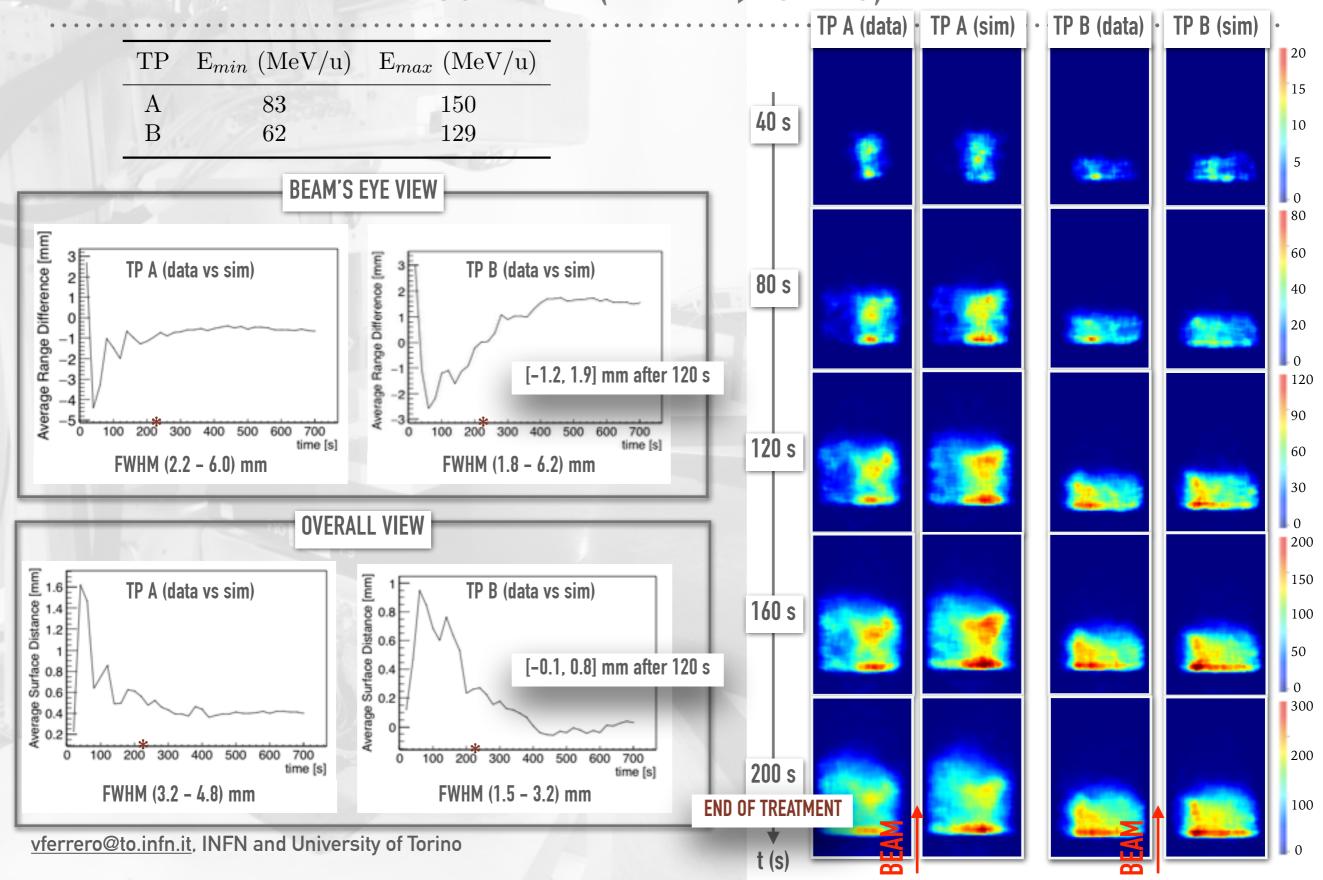
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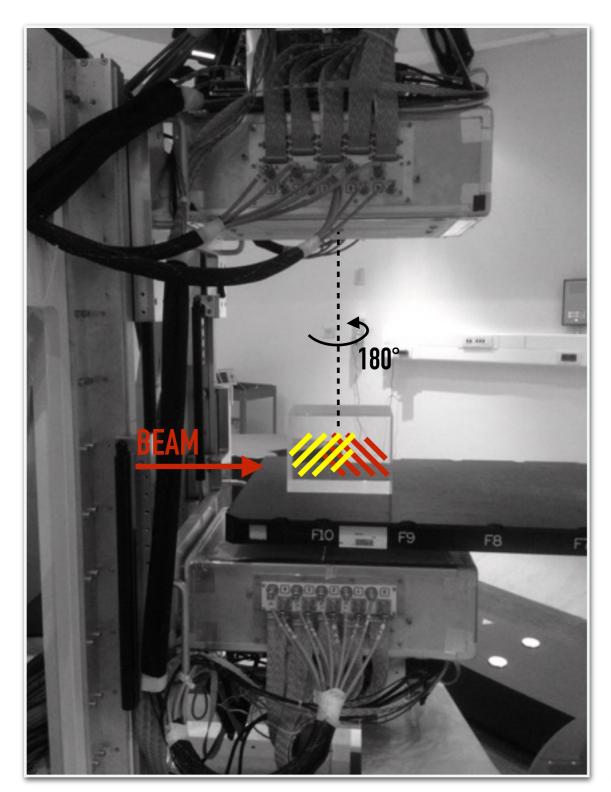
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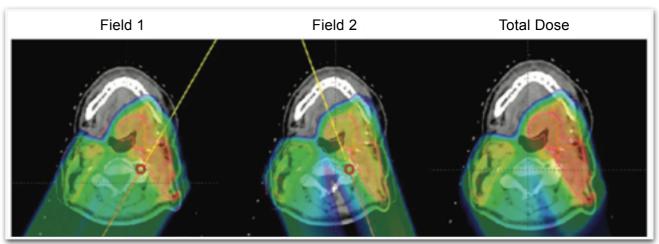


THE INSIDE PROJECT:ONLINE MONITORING AND SIMULATION VALIDATION WITH THE IN-BEAM PET SCANNER (7th YRM, TORINO)

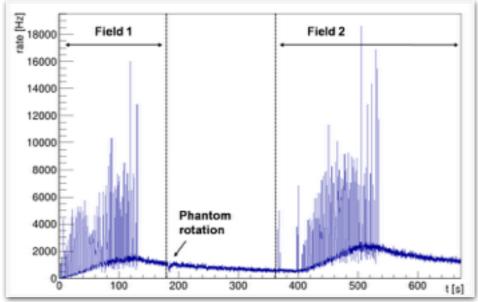


DOUBLE FIELD HADRONTHERAPY TREATMENT MONITORING WITH THE INSIDE IN-BEAM PET: PROOF OF CONCEPT ON PMMA PHANTOMS (IEEE NSS/MIC, ATLANTA, USA)



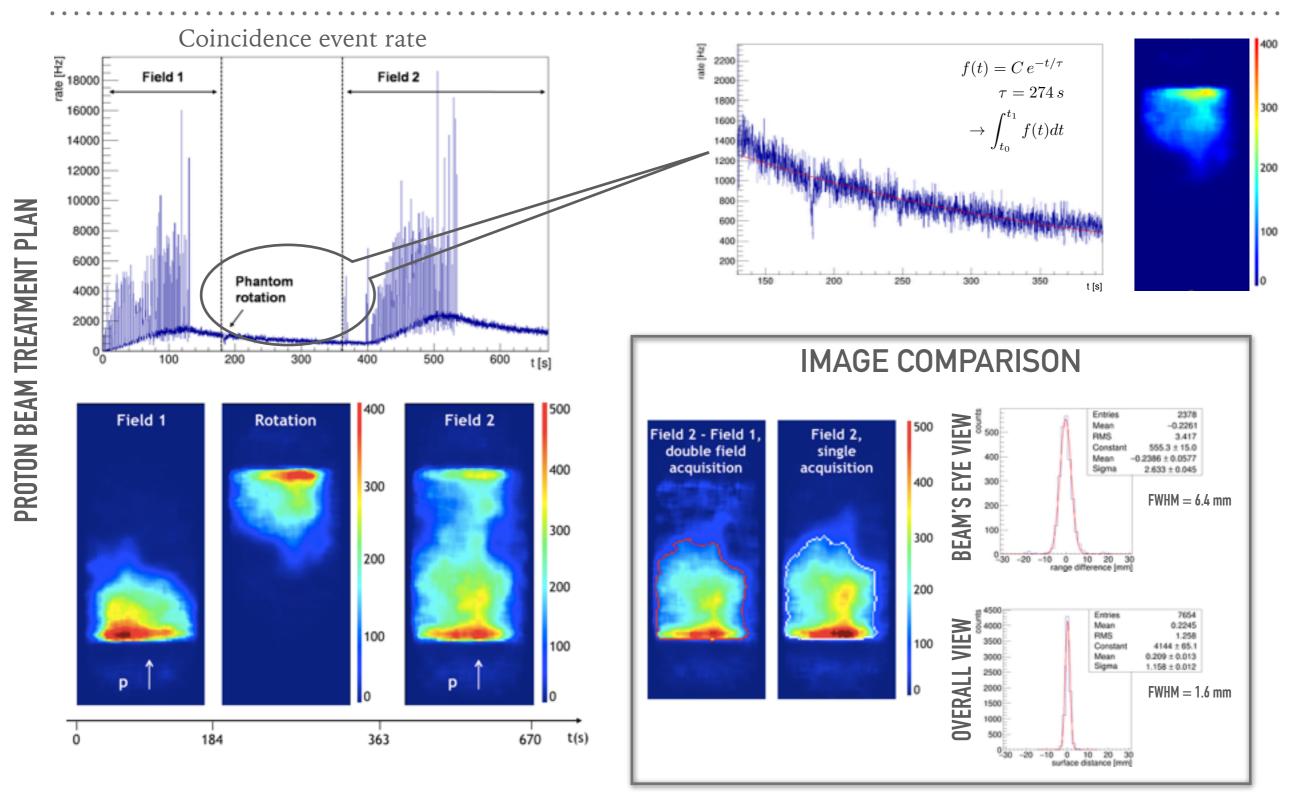


Coincidences event rate, proton beam

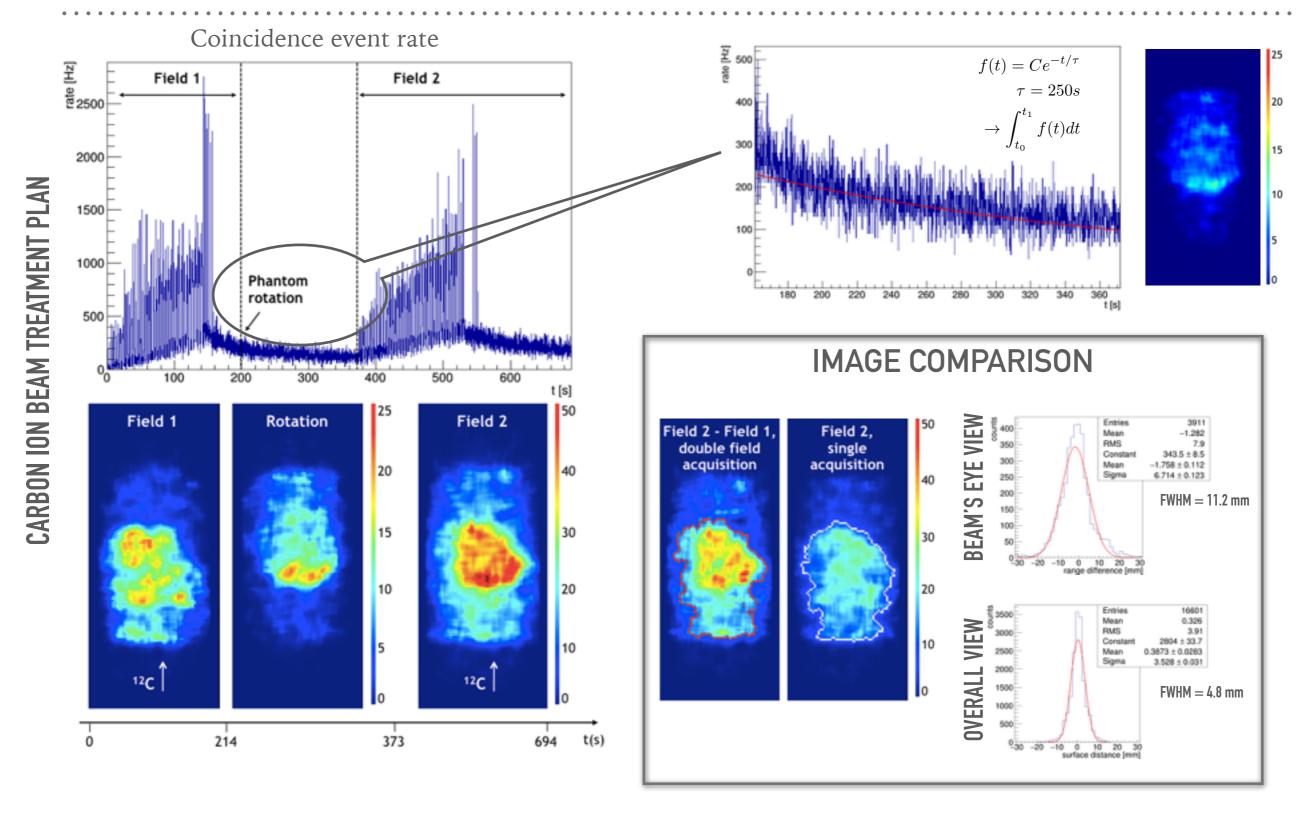


Treatment		E _{min} (MeV/u)	E _{max} (MeV/u)
Proton beam	Field 1	83	150
	Field 2	62	129
Carbon ion beam	Field 1	134	269
	Field 2	134	264

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DOUBLE FIELD HADRONTHERAPY TREATMENT MONITORING WITH THE INSIDE IN-BEAM PET: PROOF OF CONCEPT ON PMMA PHANTOMS (IEEE NSS/MIC, ATLANTA, USA)



FIRST CLINICAL TEST



NEWSLETTER 30 *Italian* National Institute for Nuclear Physics

DECEMBER 2016



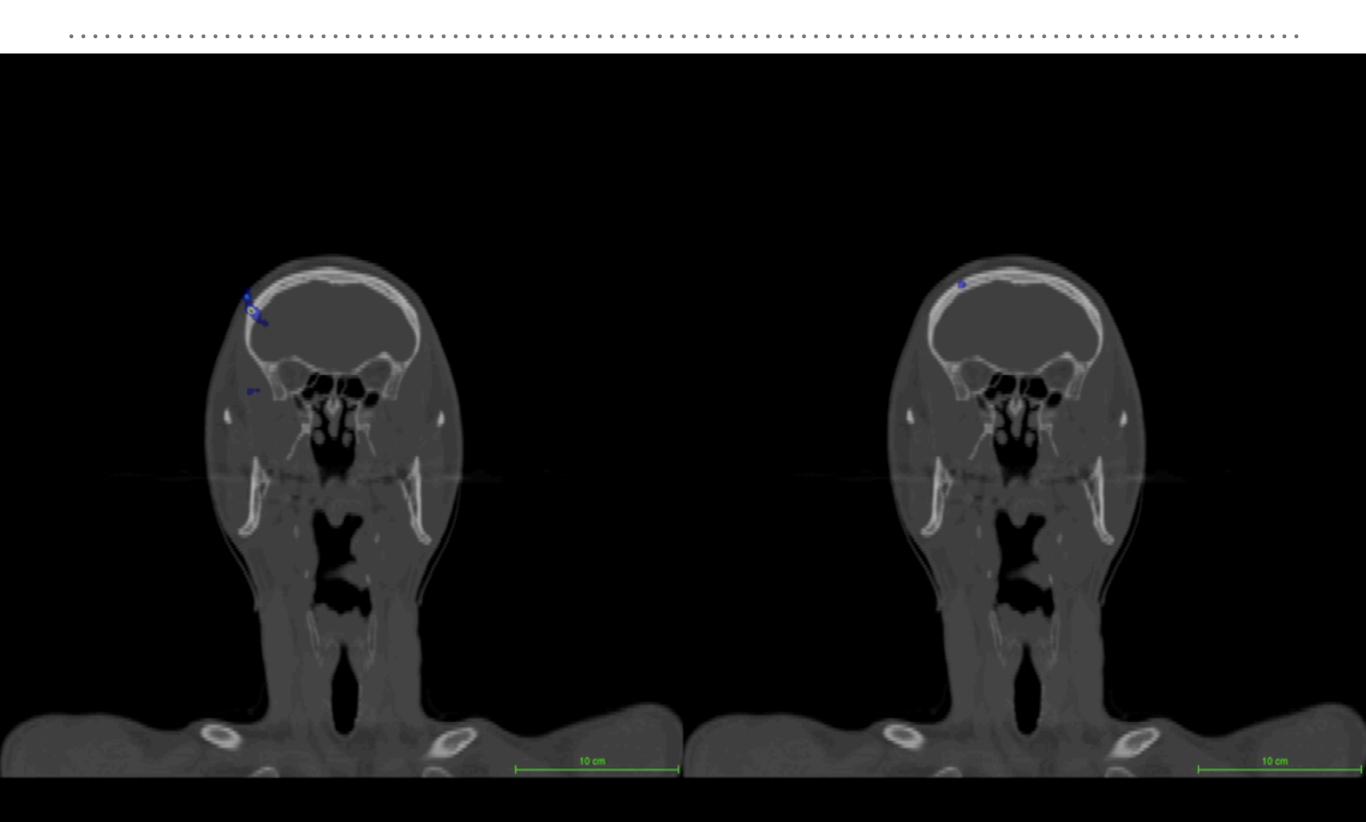
PHYSICS AND MEDICINE

CANCER: INSIDE SYSTEM SUCCESSFULLY TESTED FOR THE FIRST TIME ON A PATIENT

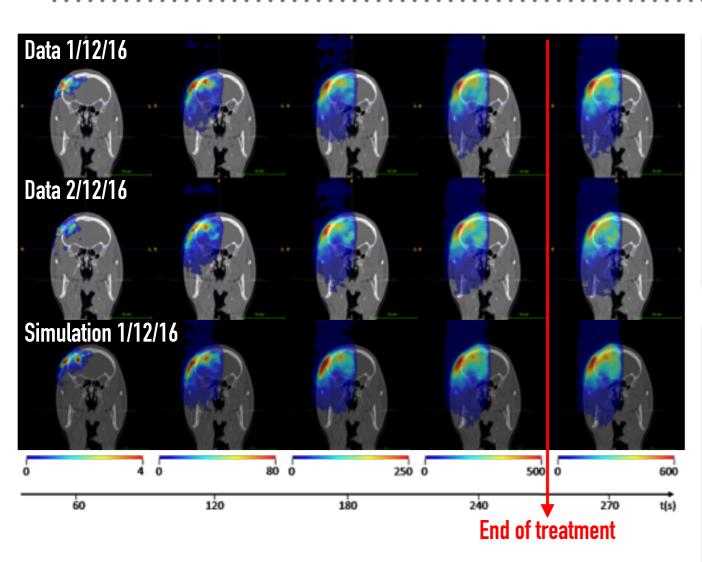
INSIDE (Innovative Solutions for Dosimetry in Hadrontherapy) has been tested for the first time on a patient. This innovative imaging system, which uses particle accelerators, was built by the INFN in

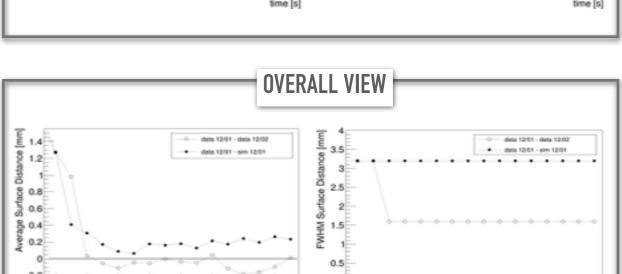
Turin to further enhance the efficacy of hadron therapy, used for the treatment of localised tumours. INSIDE, which received a € 1 million grant under the PRIN (Relevant National Interest Projects) program, is the result of a research project coordinated by the University of Pisa in collaboration with the Universities the universities of Turin and Sapienza of Rome, Bari Polytechnic University and INFN. For the trial phase, INSIDE was tested on the patient at the Italian National Centre for Oncological Hadron Therapy (CNAO), in Pavia. INSIDE is an innovative monitoring system, which uses detector technology to obtain images of what happens inside the patient's body during the hadron therapy treatment. In more detail, this bimodal imaging system combines a positron emission tomography (PET) scanner with a tracking system for charged particle imaging and is capable of operating during radiation delivery to treat head and neck tumours.

FIRST CLINICAL TEST



FIRST CLINICAL TEST





BEAM'S EYE VIEW

Comparison analysis of the experimental data acquired in the two consecutive days: Ferrero V., Fiorina E., Morrocchi M., Pennazio F. et al, Online proton therapy monitoring: clinical test of a Silicon-photodetector-based in-beam PET, submitted to Nature Scientific Reports

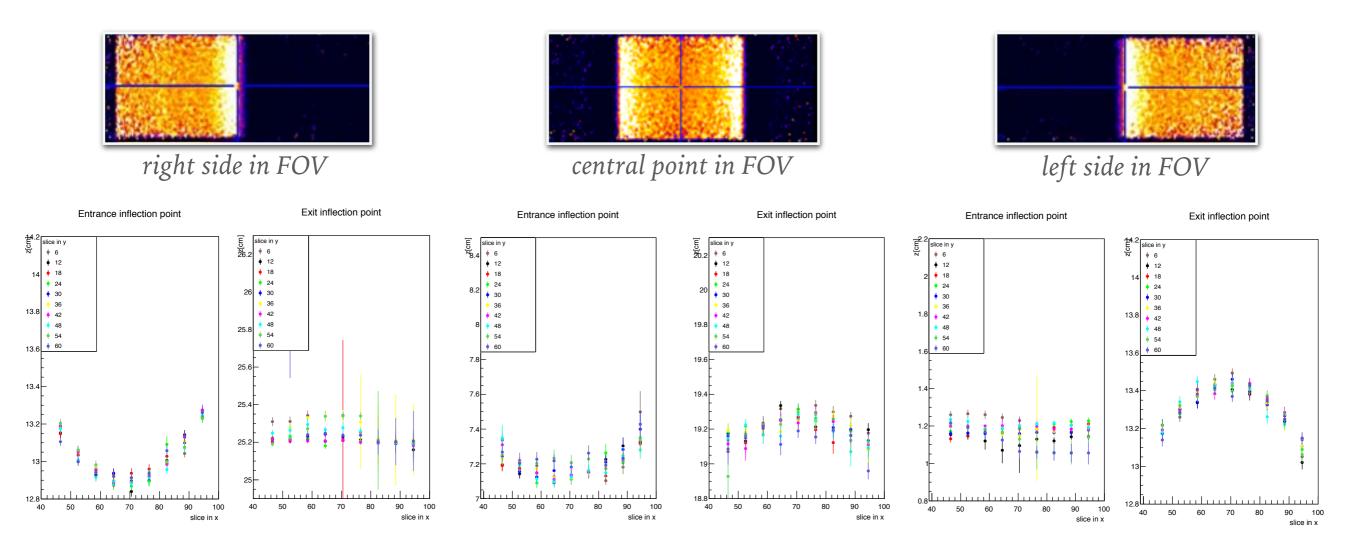
data 12/01 - data 12/02

IN THE NEXT FUTURE: RECONSTRUCTION ALGORITHM



Simulation of a 10x10x12 cm³ water phantom at different positions along z (beam axis) 30 kBq activity (¹⁸F-FDG)

Maximum Likelihood Expectation Maximization (MLEM) reconstruction model with 5 iteration



The reconstruction algorithm is limited by the PET dual head geometry, but it could be optimized, e.g, by integrating the beam information → Visiting at Lubëck University, Germany, 2018



IN THE NEXT FUTURE

- ➤ Mechanical cart upgrade
- ➤ PET/tracker combined acquisition tests
- ➤ Longitudinal clinical trials @ CNAO
- ➤ Image reconstruction algorithm: visiting period (3 months - Erasmus Traineeship grant) @ Lubëck University, Germany









PUBLISHED

CONFERENCE AND WORKSHOP PRESENTATIONS

2017

2016

IEEE NSS/MIC, Atlanta, Georgia, USA

Fisica e Informatica in Medicina, Monza, Italy

7th Young Researchers Meeting, Torino, Italy

14th Topical Seminar on Innovative Particle and Radiation Detectors, Siena, Italy

102° Italian National Congress, Padua, Italy

PAPERS

The INSIDE project: in-beam pet scanner system features and characterization. Journal of Instrumentation, 12(03):C03051, 2017.

The INSIDE project: on-line monitoring and simulation validation with the in-beam PET scanner. Journal of Physics: Conference Series, 841(1):012011, 2017.

INSIDE in-beam positron emission tomography system for particle range monitoring in hadrontherapy. Journal of Medical Imaging, 4(1), 2016.

Full-beam performances of a pet detector with synchrotron therapeutic proton beams. Physics in Medicine and Biology, 61(23):N650-N666, 2016.

First results of the INSIDE in-beam pet scanner for the on-line monitoring of particle therapy treatments. Journal of Instrumentation, 11(12):C12011, 2016.

SUBMITTED

Online proton therapy monitoring: clinical test of a Silicon-photodetector-based in-beam PET, Nature Scientific Reports

ORK IN ROGRESS

Monte Carlo Simulations and data analysis of carbon ions beam therapy monitoring: a case study with the INSIDE in-beam PET

Monte Carlo simulation tool for online treatment monitoring in hadrontherapy with in-beam PET

Double-field hadrontherapy treatment monitoring with the INSIDE in-beam PET: proof of concept on PMMA phantoms