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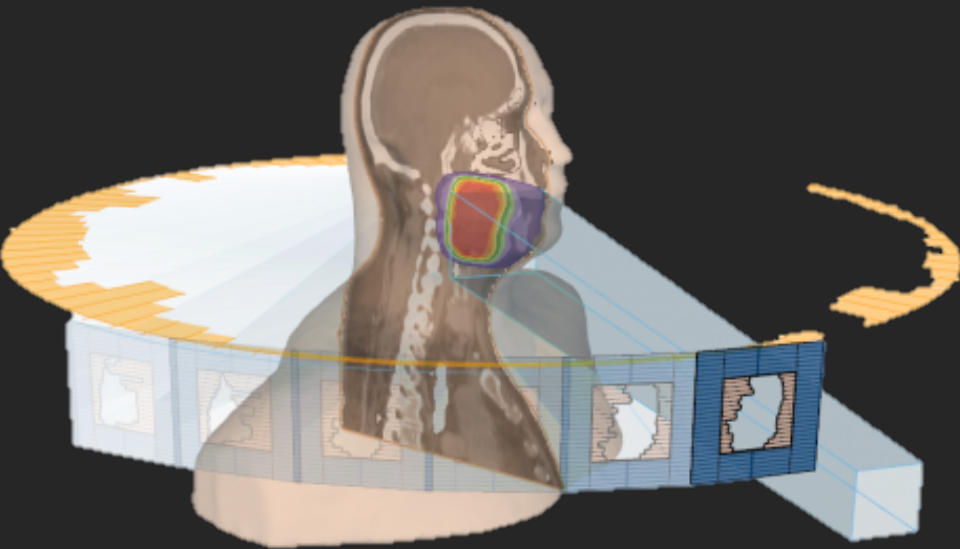
Fisica e medicina: utilizzo della PET in adroterapia

Incontri di Fisica dell'Area Pontecorvo
Aula Magna "Fratelli Pontecorvo"
Pisa, 24/5/2017

La radioterapia

La radioterapia e' una tecnica che utilizza le radiazioni ionizzanti per la cura dei tumori.

Le radiazioni dirette contro la massa tumorale, danneggiano il DNA delle cellule bloccandone la crescita e la replicazione.

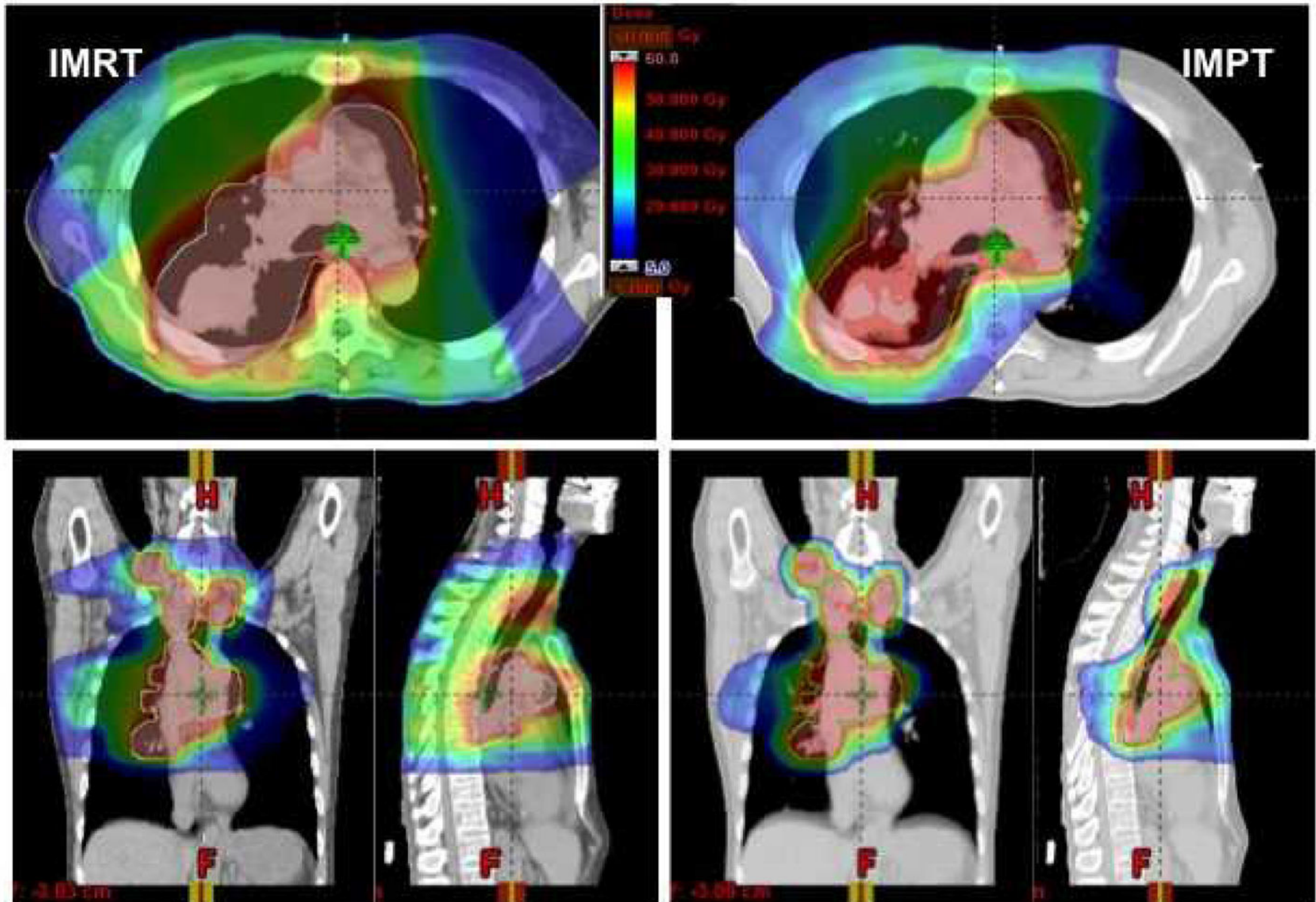


L'adroterapia

L'adroterapia è una particolare forma di radioterapia che utilizza particelle cariche pesanti (protoni e ioni carbonio) invece della radiazione convenzionale (fotoni ed elettroni)



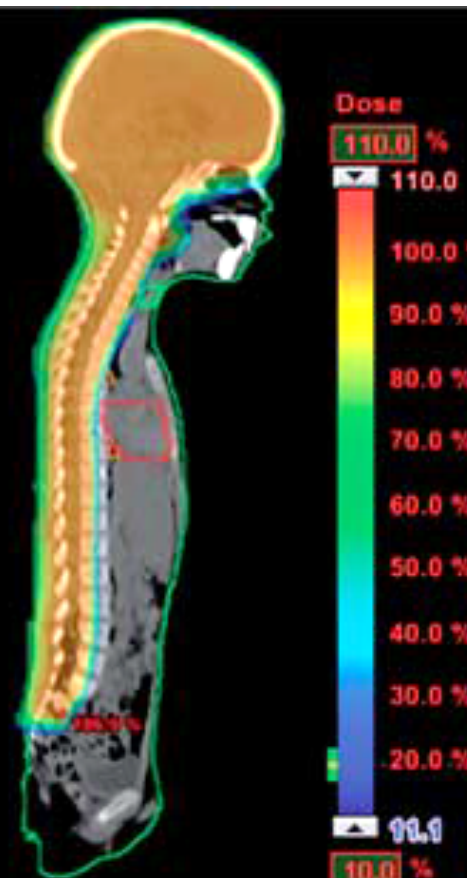
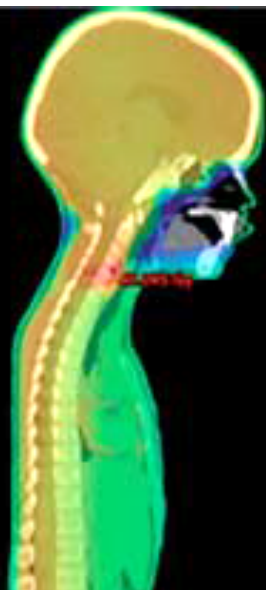
PERCHE' L'ADROTERAPIA



3D-CRT

IMRT

IMPT

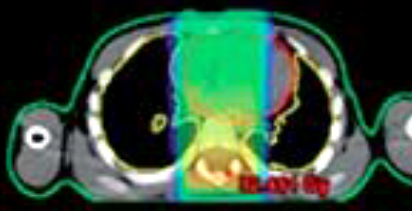


Review

Dosimetric Comparison and Potential for Improved Clinical Outcomes of Paediatric CNS Patients Treated with Protons or IMRT

Kris S. Armoogum^{1,†,*} and Nicola Thorp^{2,†}

Cancers 2015, 7, 706-722;



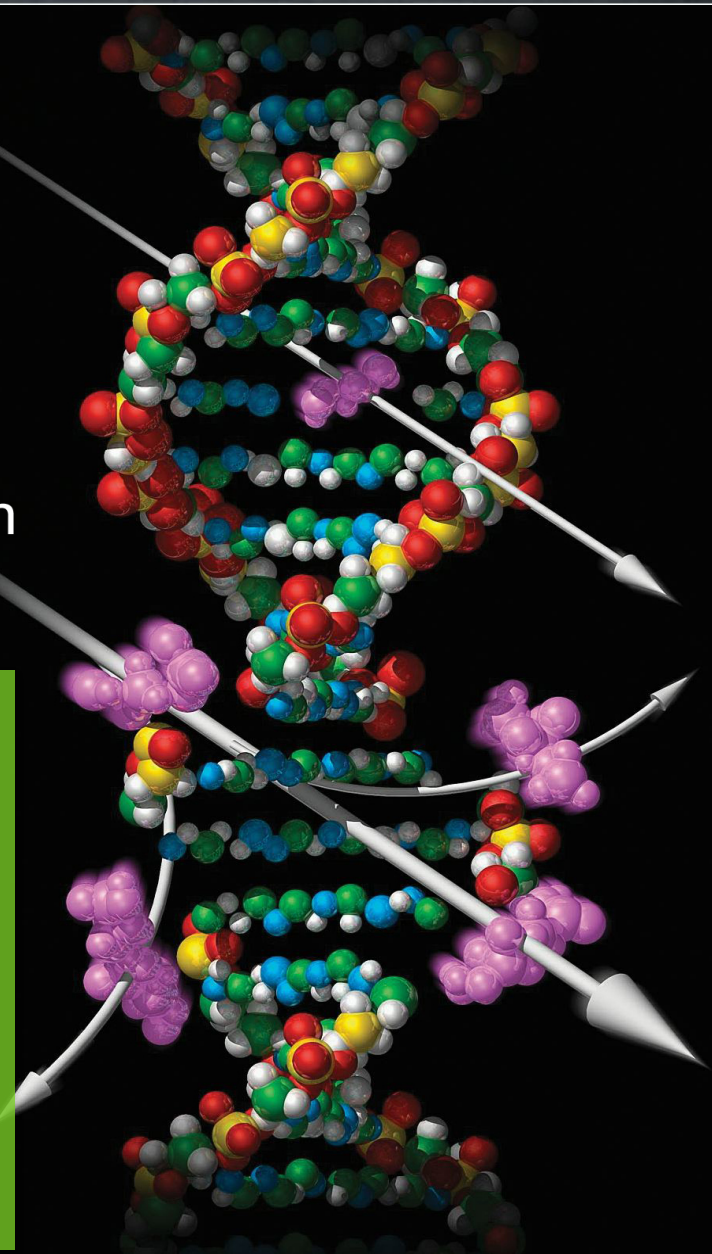
ependymoma. *Results:* This review found that while proton beam therapy offered similar clinical target coverage, there was a demonstrable reduction in integral dose to normal structures. *Conclusions:* This in turn suggests the potential for superior long term outcomes for paediatric patients with CNS tumours both in terms of radiogenic second cancers and out-of-field adverse effects.

Efficacia Biologica



X-ray
track

Heavy-ion
track

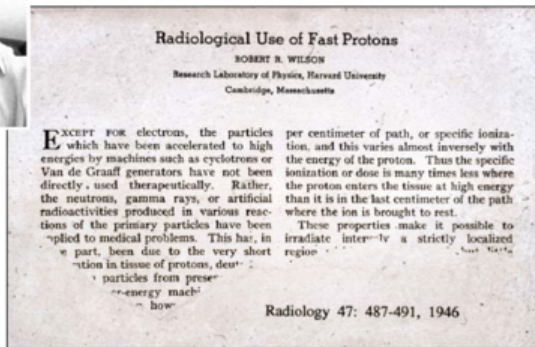


L'elevata dose depositata dagli ioni (ad es. Carbonio) per unita' di percorso e' correlata con una maggiore efficacia biologica rispetto a quella di protoni e radiazioni convenzionali

Proposta da R. R. Wilson, 1946

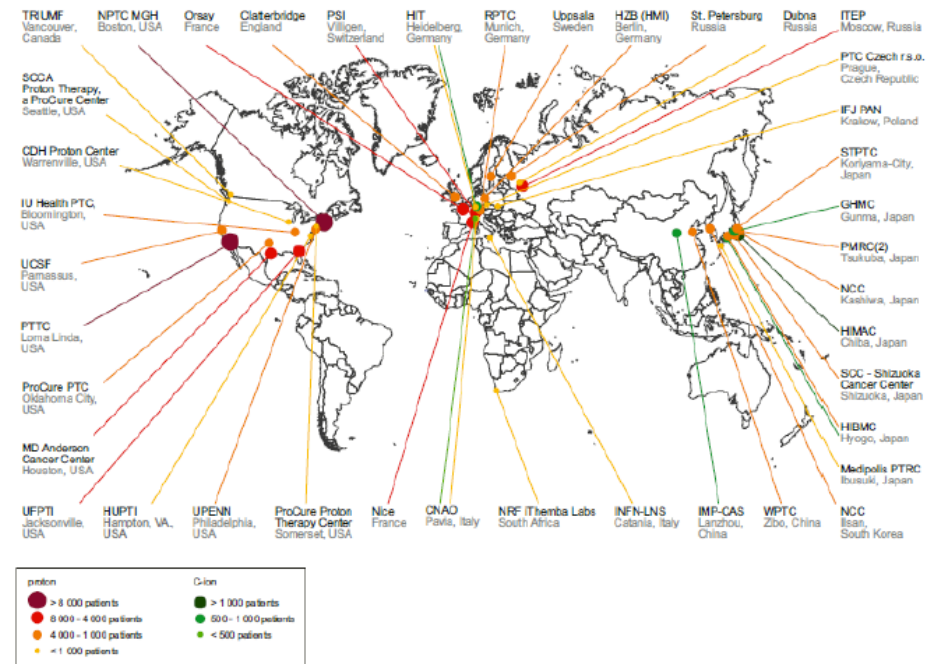


R.R. Wilson, "Foreword to the Second International Symposium on Hadrontherapy," in *Advances in Hadrontherapy*, (U. Amaldi, B. Larsson, Y. Lemoigne, Y., Eds.), Excerpta Medica, Elsevier, International Congress Series 1144: ix-xiii (1997).



- 1st patient treated with proton beams in 1954 (since 1990 more than 100000 pts so far)
- since 1994, more than 15000 pts treated using carbon ions (NIRS Chiba, GSI, ...)
- 52 proton facilities in operation (15 in Europe) e 10 using carbon ions (3 in Europe)
- facilities under construction or in planning stage: 48 protons (15 in Europe) e 3 carbon ions (1 in Europe)

<https://www.ptcog.ch/>, dati aprile 2017



In Italia 3 centri clinici
 CATANA (INFN-LNS, 2002)
 CNAO (2011)
 Centro Protonterapia Trento (2014)
 Nel marzo 2017 l'adroterapia e' stata inserita nei Livelli Essenziali di Assistenza (LEA)

Il Cnao è una struttura ospedaliera e di ricerca unica in Italia, nata per curare con l'adroterapia pazienti affetti da tumori solidi radioresistenti e difficilmente operabili. Dal 2011 ad oggi sono stati trattati piu' di 1000 pazienti.

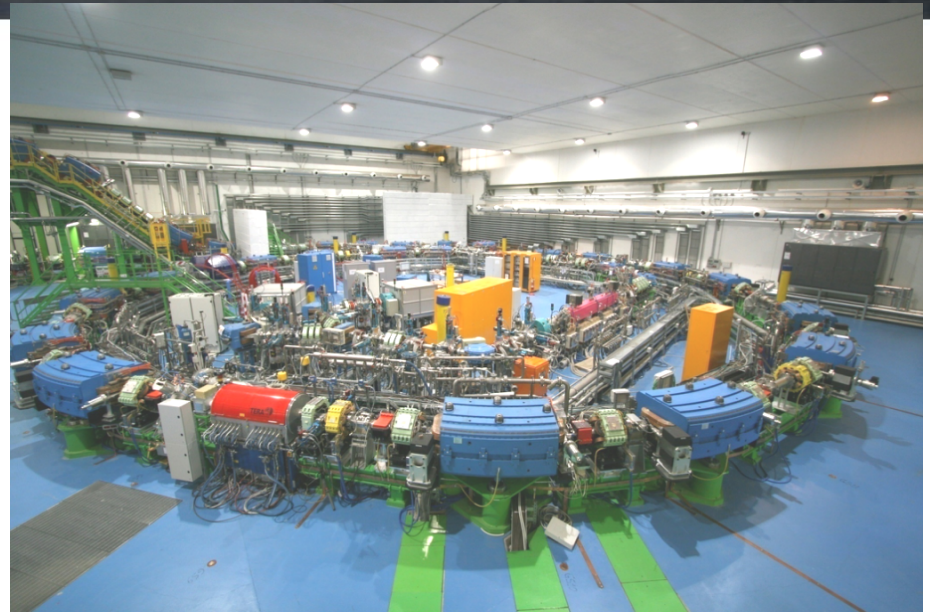
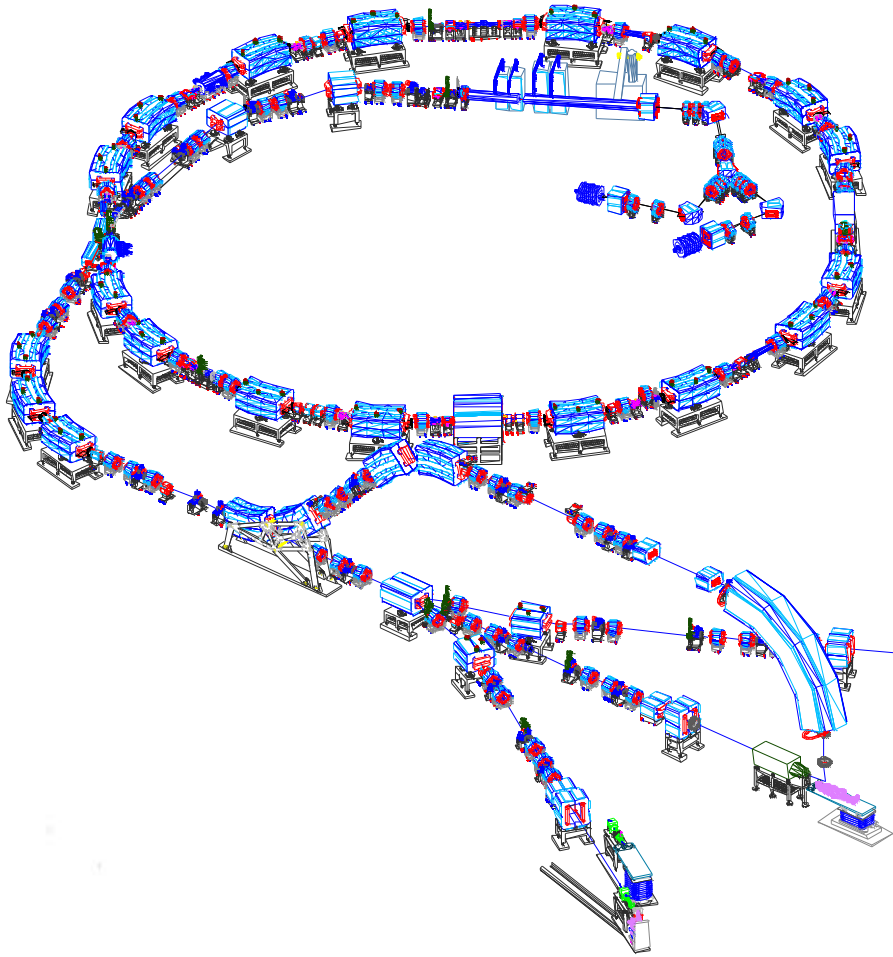


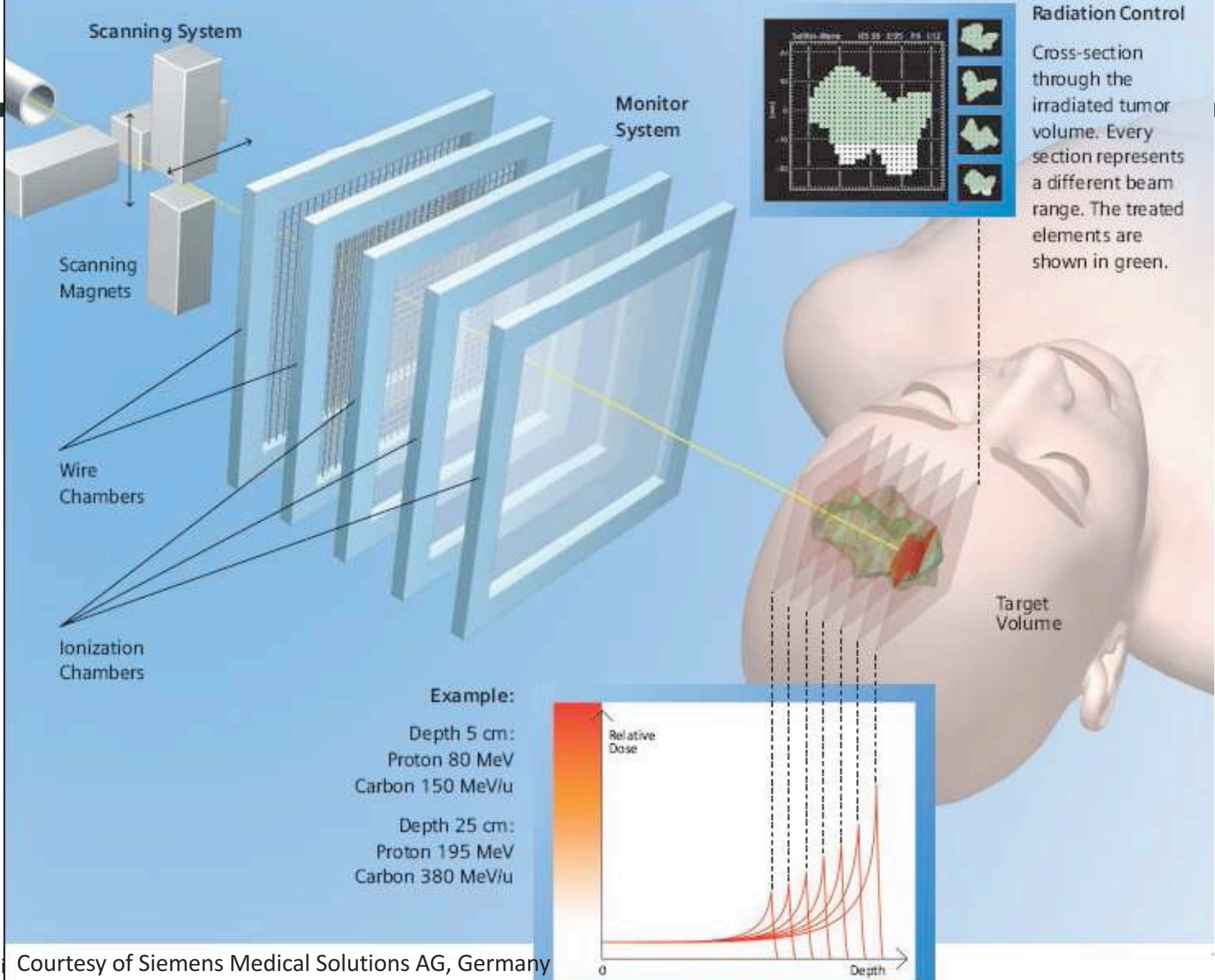
Centro Nazionale Adroterapia Oncologica



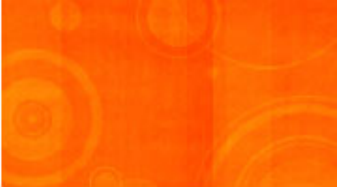
fondazione **CNAO**

Synchrotron-based facility

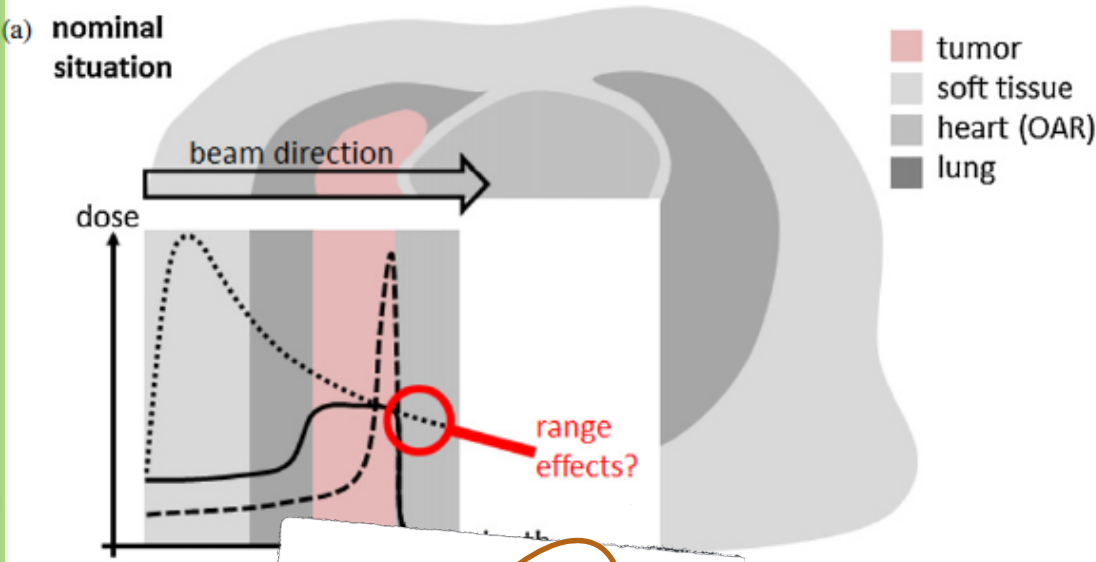




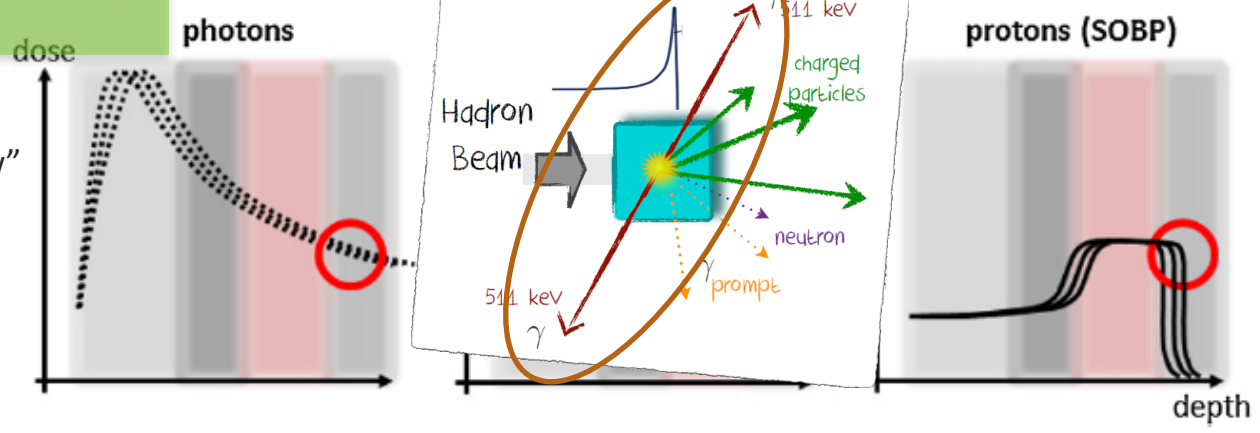
INCERTEZZA SUL RANGE DELLE PARTICELLE



Una delle principali limitazioni dell'adroterapia e' la sua estrema sensibilita' alle incertezze legate alla profondita' di penetrazione degli ioni in tessuto (range)



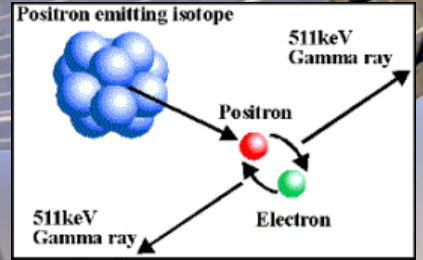
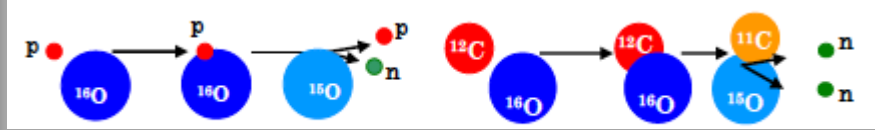
(b) "uncertain" situation



Antje-Christin Knopf and Antony Lomax.,
"In-vivo proton range verification: a review"
Phys. Med. Biol. 58 (2013) R131-R160

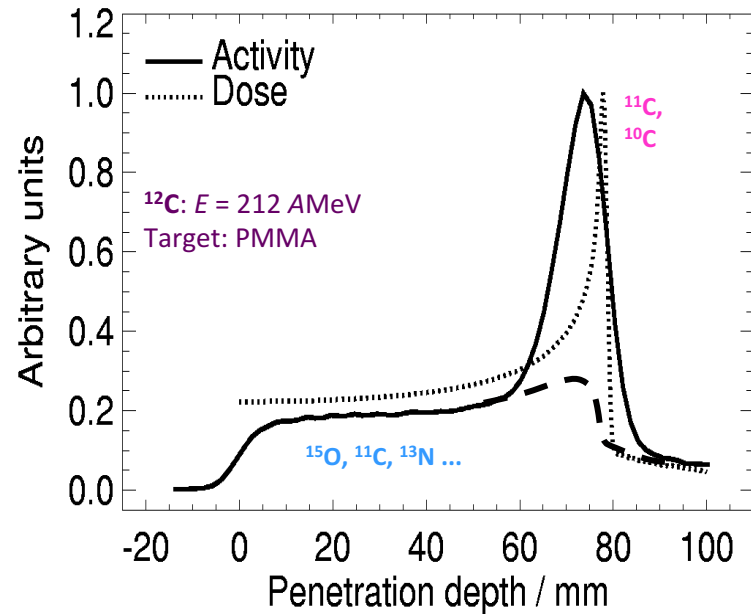
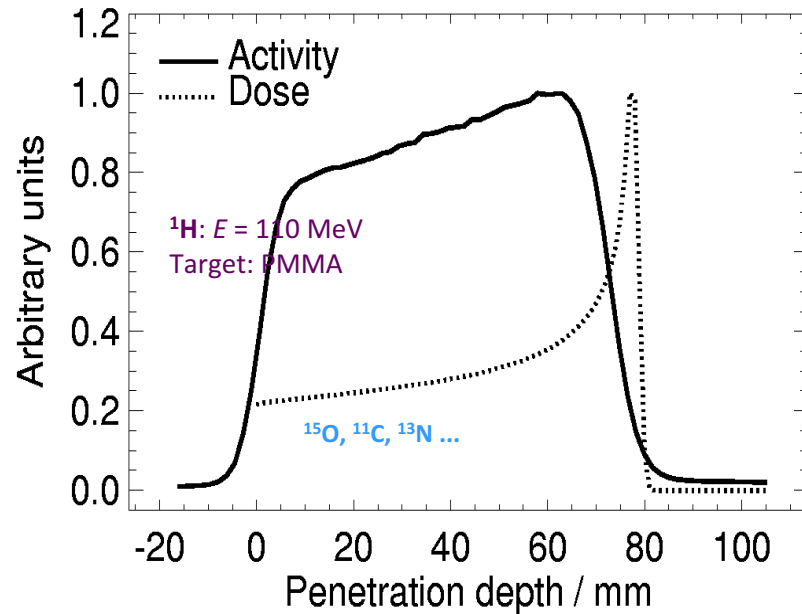
"Vedere" cosa viene trattatato

La tecnica piu' usata per monitorare "in-vivo" il percorso degli ioni e' la Tomografia ad Emissione di Positroni (PET), che permette di misurare l'attivita' di radionuclidi emettitori di positroni (beta+) prodotti in seguito ad interazioni nucleari del fascio con i tessuti attraversati.



■ POSITRON EMISSION TOMOGRAPHY

PET monitoring: complicazioni

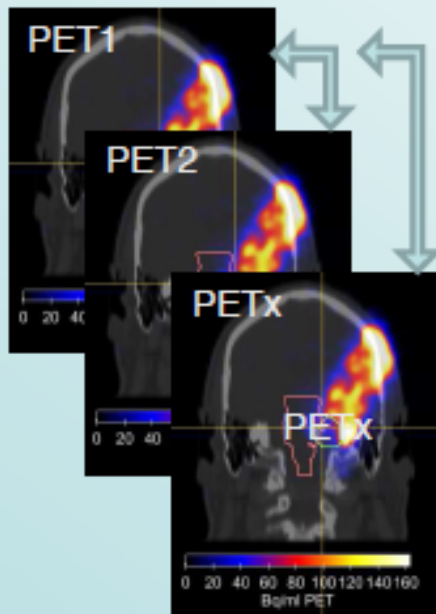


ATTIVITA' \neq DOSE

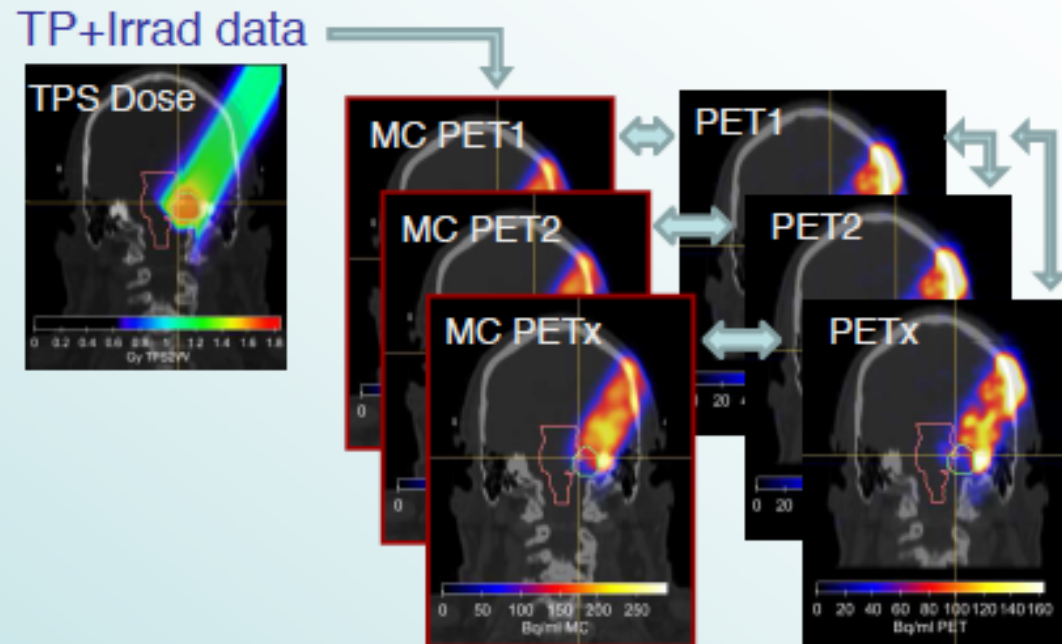
J Pawelke et al., Proceeding: Ion Beams in Biology and Medicine (IBIBAM), 26.-29.09.2007, Heidelberg, Germany

PET Monitoring e verifica del trattamento

Inter-fractional comparison:
 $PET_x - PET_1$
→ **Reproducibility**

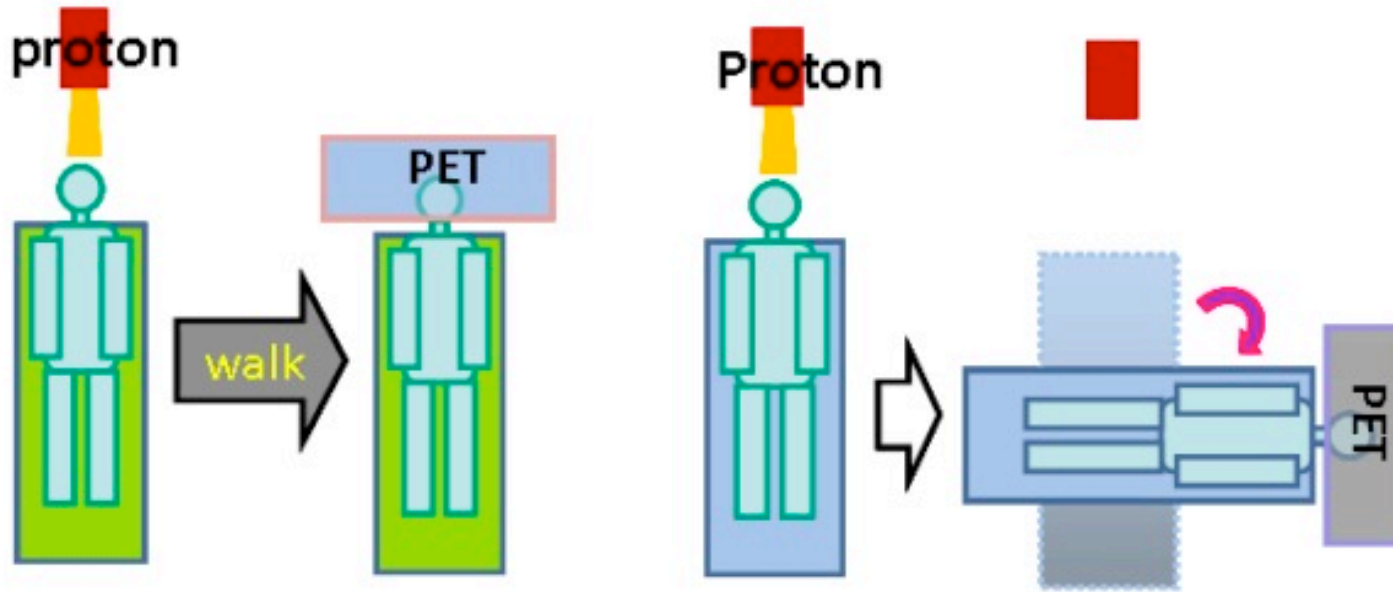


Comparison to expectation (MC):
 $MC PET_x - PET_x$
→ **Accuracy & Reproducibility**



Courtesy of J. Bauer, HIT

Diverse realizzazioni

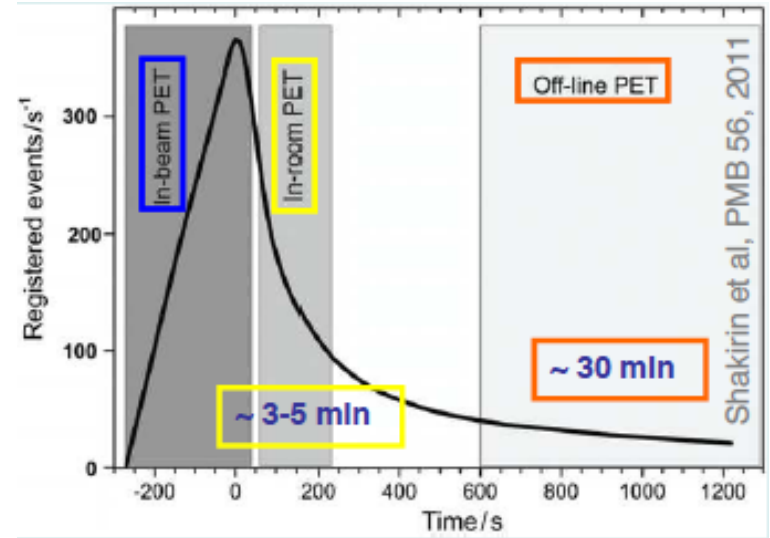


- Off-room PET
 - HIMA, Chiba, Japan
 - Proton Therapy Institute in Florida, USA
 - Heidelberg Ion Therapy Center (HIT)

- In-room PET
 - neuroPET (now full PET ring integrating CT) at MGH, USA

PET monitoring: complicazioni

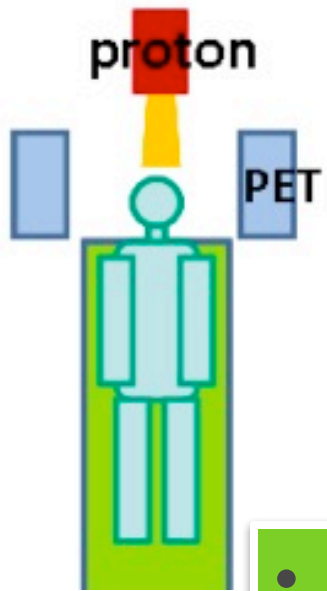
- Radioisotopi β^+ a breve emivita
 - ^{11}C (20.3 min), ^{13}N (9.97 min), ^{15}O (2.03 min).
- Bassi livelli di attivita' prodotta



Therapy beam	^1H	^3He	^7Li	^{12}C	^{16}O	Nuclear medicine
Activity density / $\text{Bq cm}^{-3} \text{Gy}^{-1}$	6600	5300	3060	1600	1030	$10^4 - 10^5 \text{Bq cm}^{-3}$

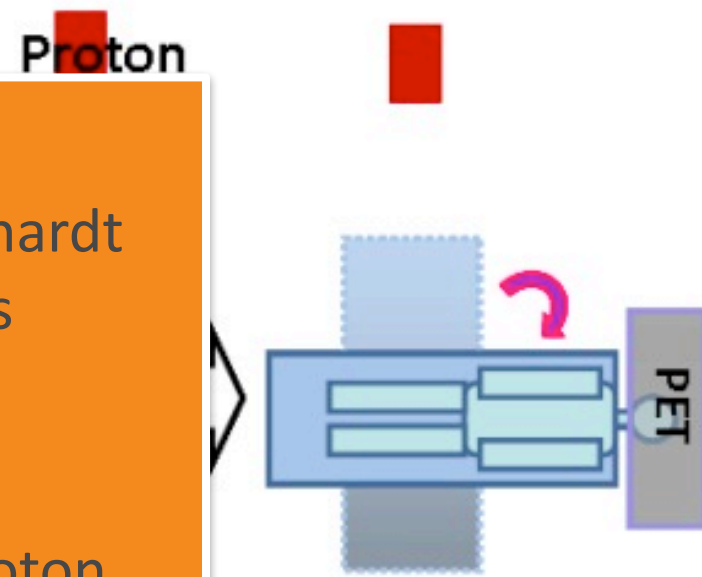
- Wash-out

Diverse realizzazioni



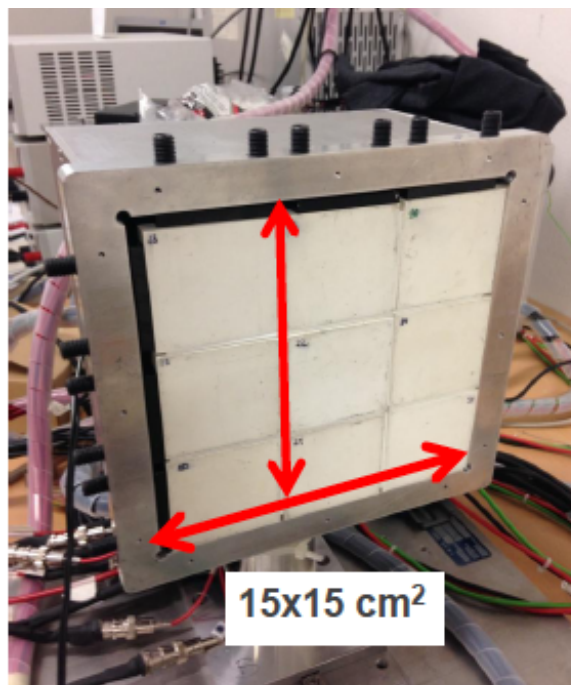
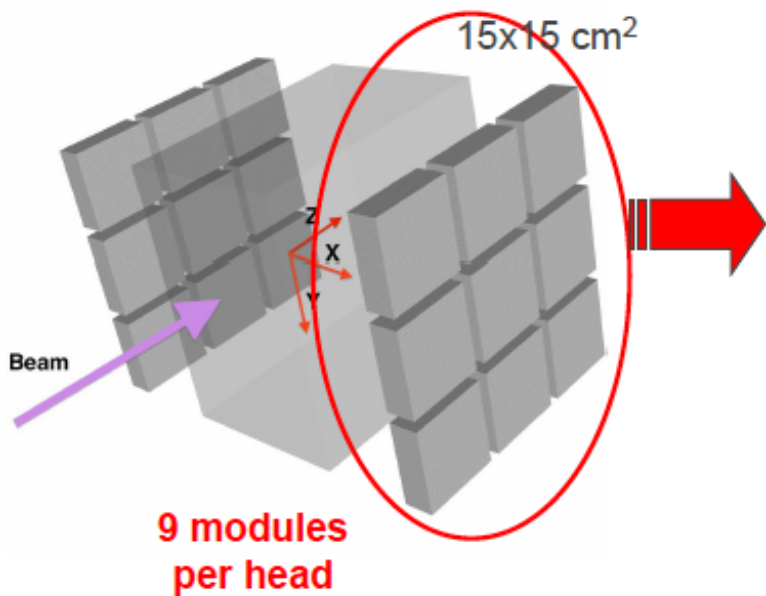
- In-beam PET
 - First pioneer work by Enghardt et al. In the '90 with C ions (GSI/Bastei Tomograph)
 - HIMA, Chiba, Japan
 - NCC, Kashiwa, Japan w proton beams
 - “OpenPET”, NIRS, Japan
 - DoPET, INSIDE

- In Florida, USA
 - Heidelberg Ion Therapy Center (HIT)



- In-beam PET
 - PET (now full PET integrating CT) at SA

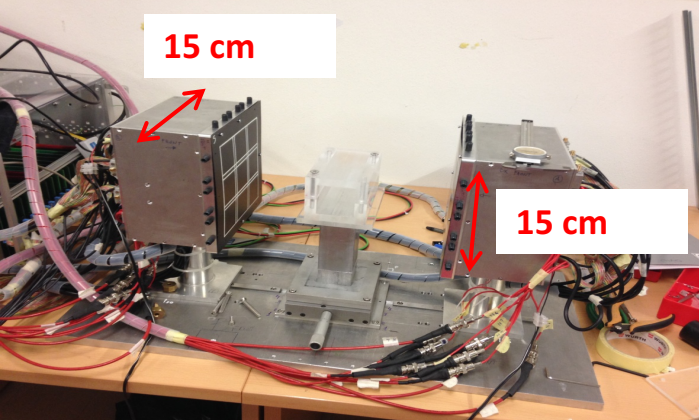
DOPET: an in-beam PET monitor for particle therapy



- Two planar PET heads
- The total size is 15 cm × 15 cm
- In-beam operation
- Portable

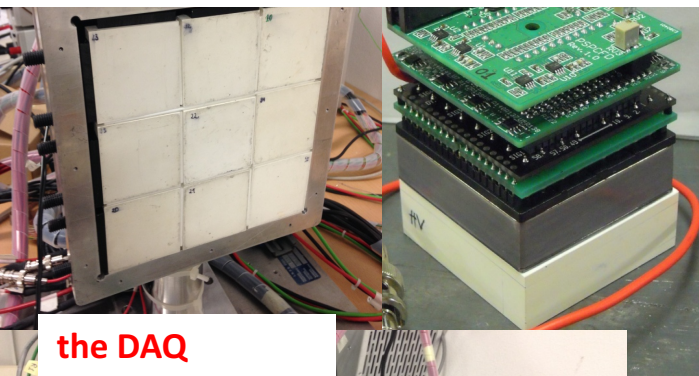
V. Rosso
University and INFN
Pisa, INFN RDH
experiment

DoPET: 15 cm x 15 cm prototype



9 detecting modules

the single module



the DAQ



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

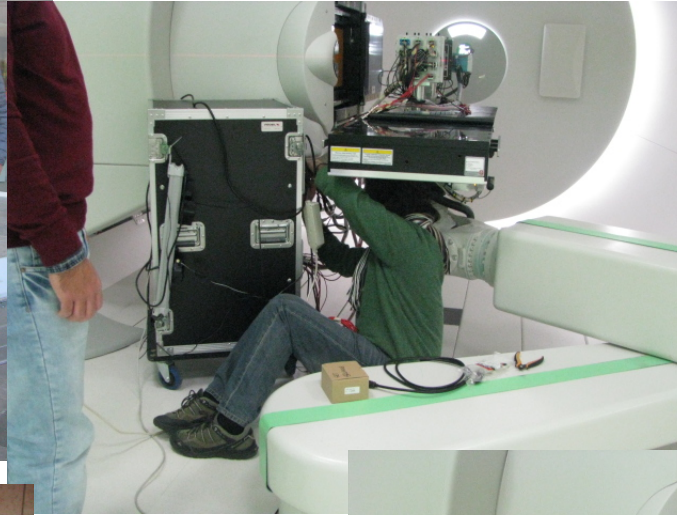
The reconstruction is performed in less than 1 minute (8 core Intel Xeon e5620 @2.4 GHz)

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

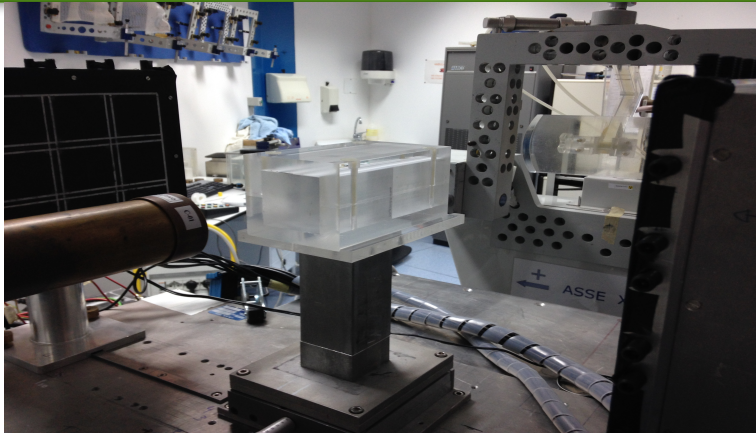
the DoPET system @ Trento



Ready for data taking in 30' !

DoPET performed several data taking

CATANA

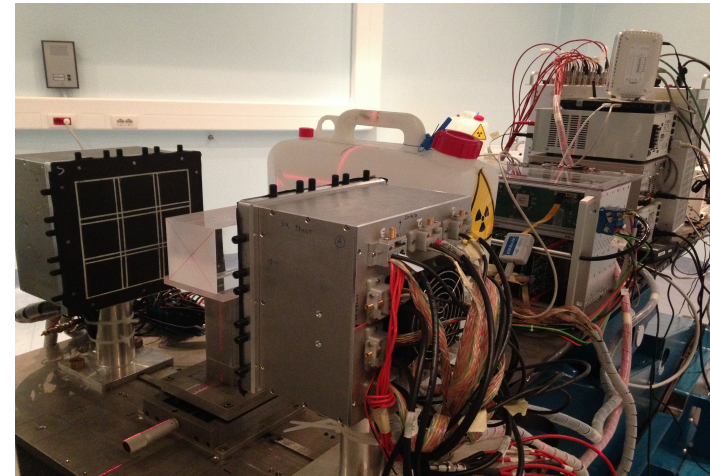


A. Kraan et al., *Physica Medica* 30 (2014) 559-569

V. Rosso et al., 2016_JINST_11_C12029

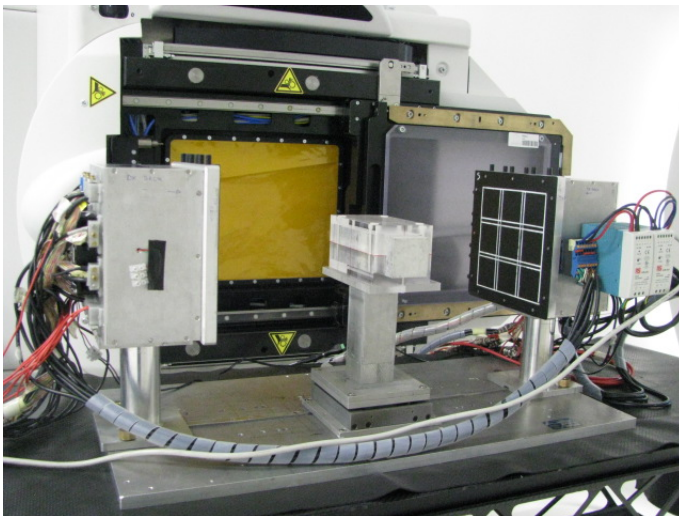
G. Sportelli et al., *JINST*, 10, C12029 (2015) 1-11

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



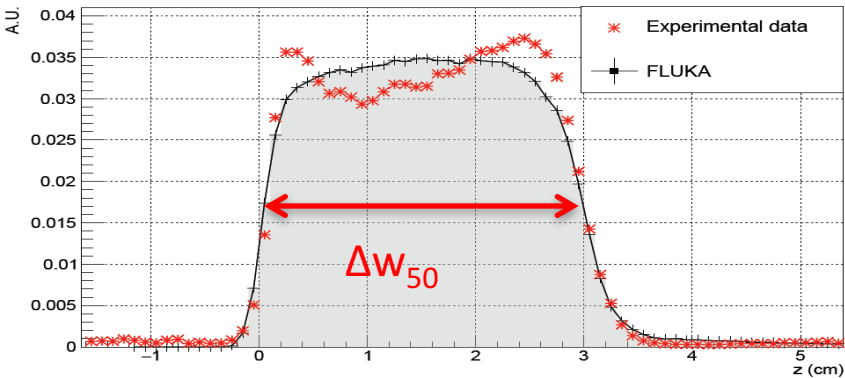
CNAO

TRENTO



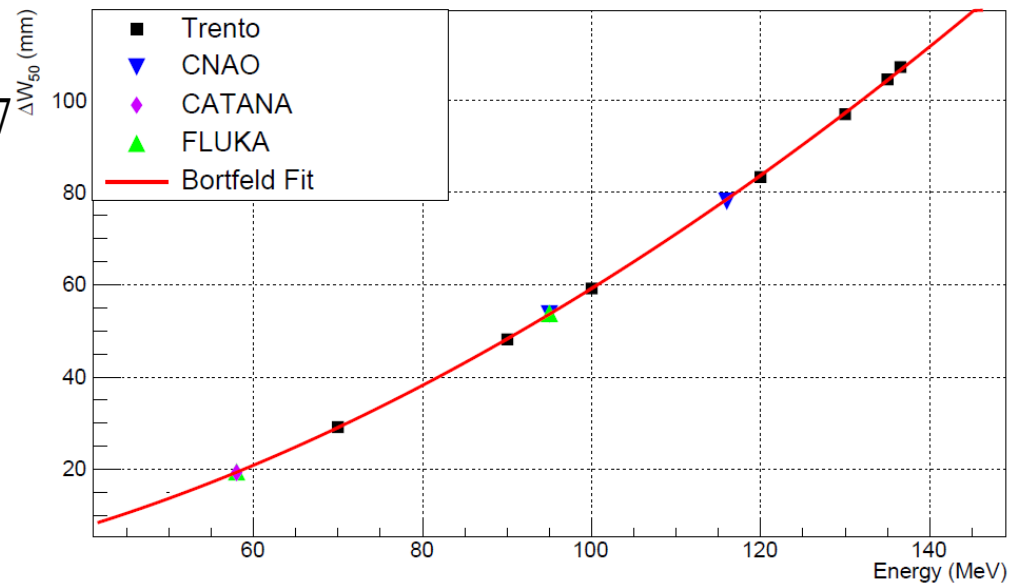
Center	Particle	Energy	Accelerator type	Collimation
CATANA	Protons	62 MeV	Cyclotron	passive
CNAO (Pavia)	Protons/ C-ions	Up to 230MeV	Synchrotron	active
Trento	Protons	Up to 230Mev	Cyclotron	active

Interconfronti tra i tre centri di adroterapia italiani



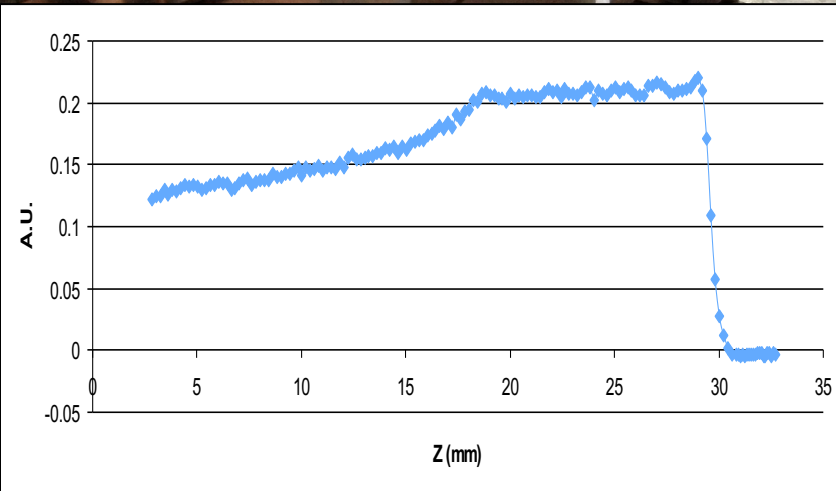
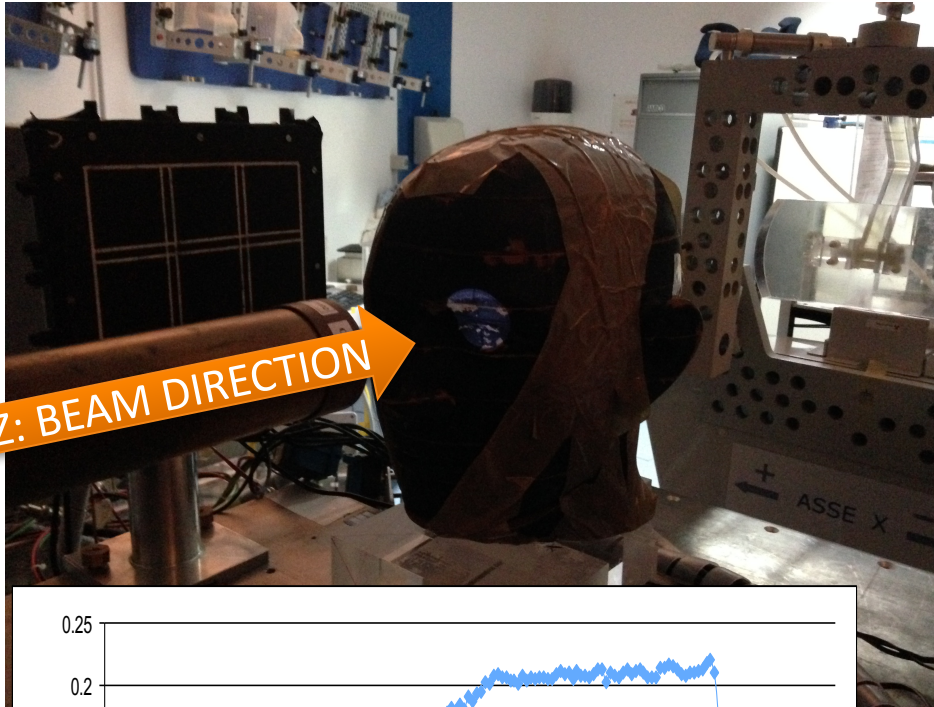
$$\Delta w_{50} = -5,15 + 0.02 E_0^{1.77}$$

- The system is easy to move
- Data are reproducible



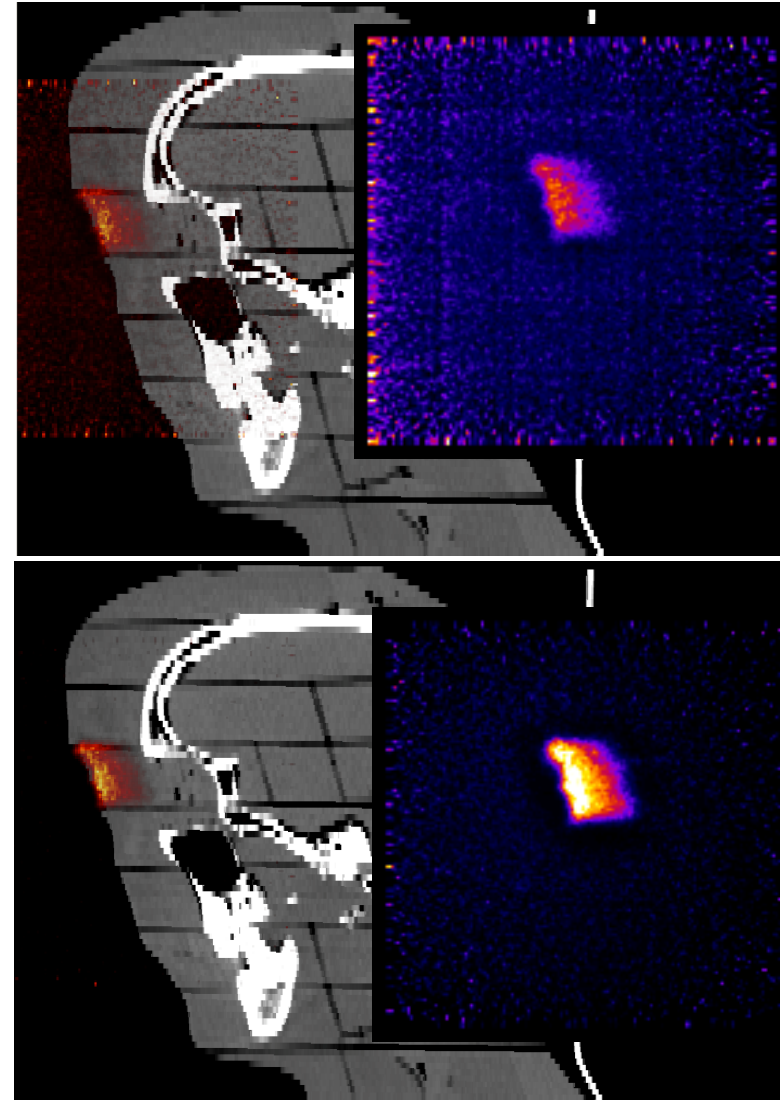
Antropomorphico phantom irradiation

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

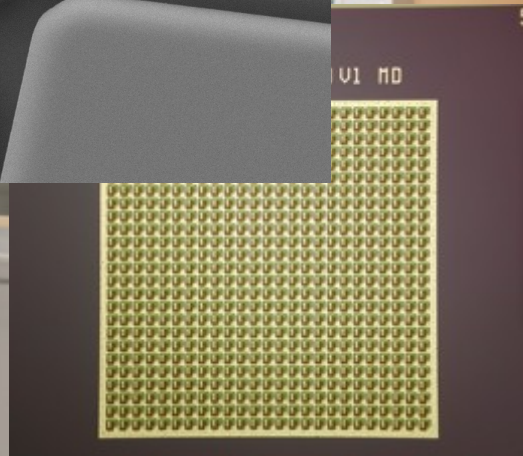
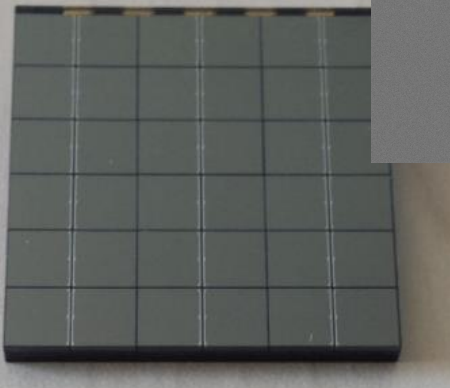
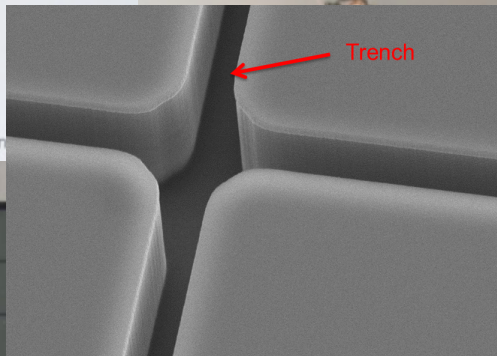
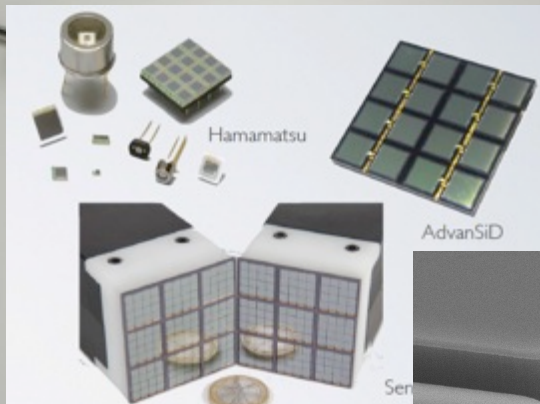


In & after treatment
0-190 s
after treatment
70-600 s

SAGITTAL VIEW

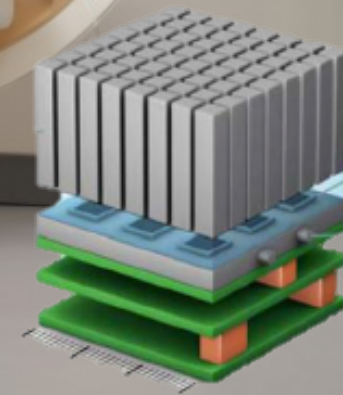


La tecnologia PET e' in continua evoluzione

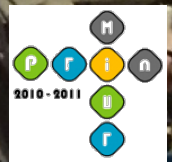


Gli occhi per “vedere” la radiazione emessa dal paziente sono costituiti da cristalli scintillanti e da tubi a vuoto che trasformano la luce in segnale elettrico

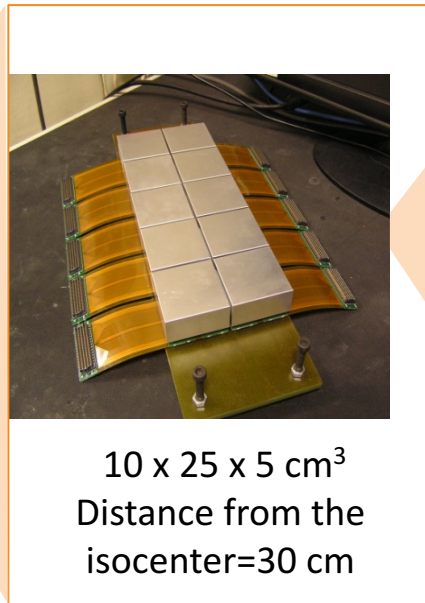
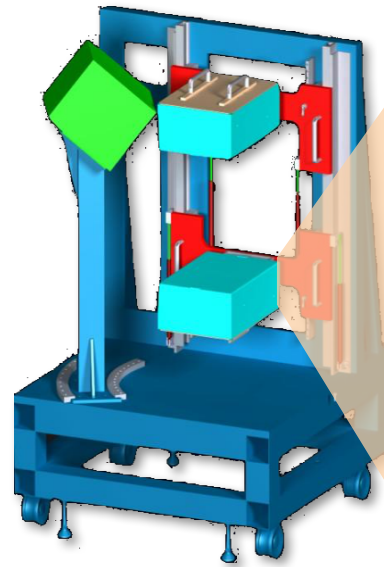
La ricerca e' rivolta verso nuovi rivelatori a semiconduttore, i fotomoltiplicatori al silicio (SiPM), che con le loro caratteristiche di compattezza e velocita' hanno fatto compiere alla tecnologia della PET un nuovo salto di qualita'



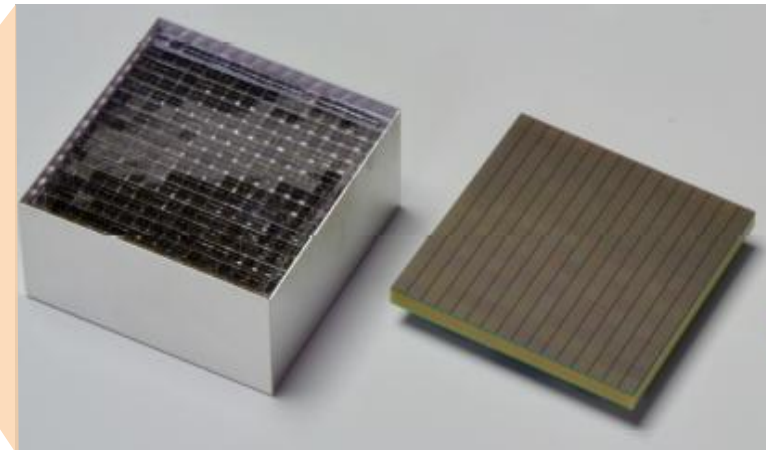
Sistema di imaging bi-modale basato sulla combinazione di uno Scanner in-beam PET e di un tracciatore di particelle cariche. Lo scopo e' misurare, entro una sessione di trattamento, il range degli ioni in tessuto e verificarne l'accordo con il valore atteso



In-beam PET Panels

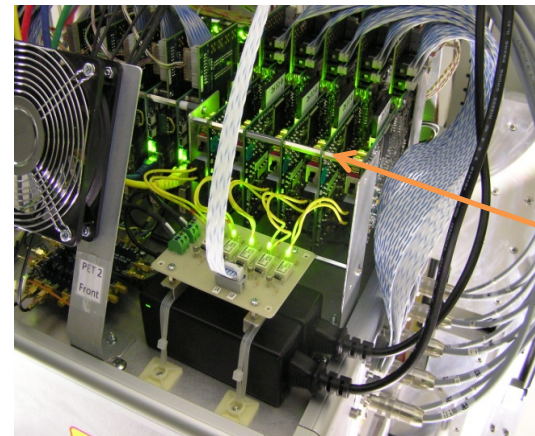
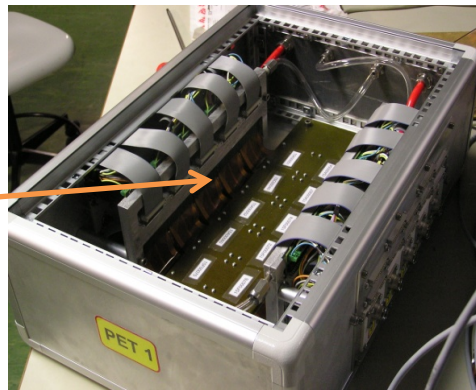


10 x 25 x 5 cm³
Distance from the isocenter=30 cm



256 LFS pixel crystals (3x3x20mm³) coupled one to one to MPPCs (Multi Pixel Photon Counters, SiPMs).

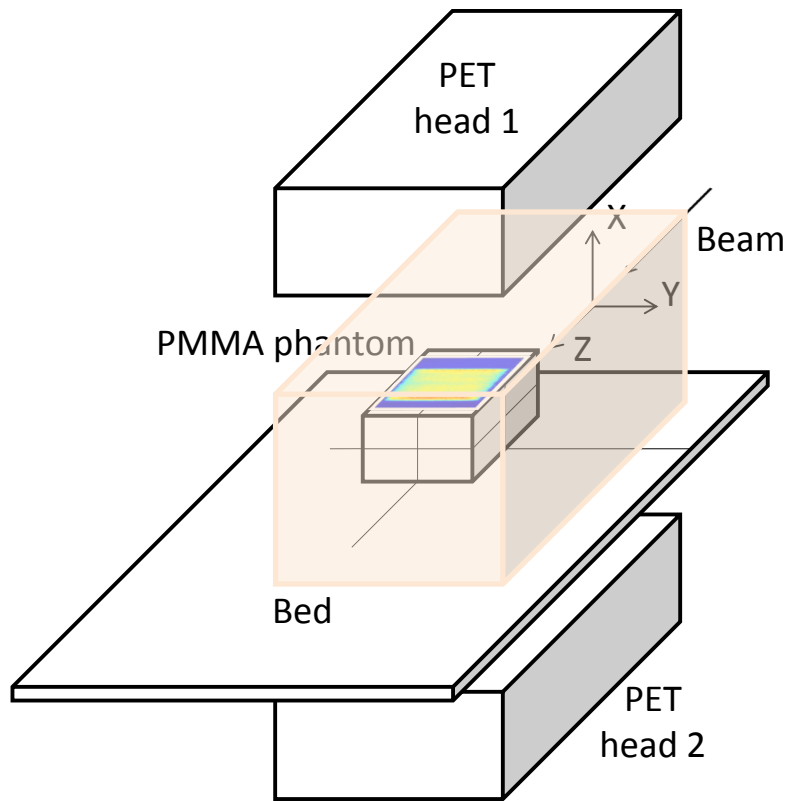
20xFE board
(4 Tofpet ASIC^[1] each)



20xFPGA Xilinx
Spartan6-SP605

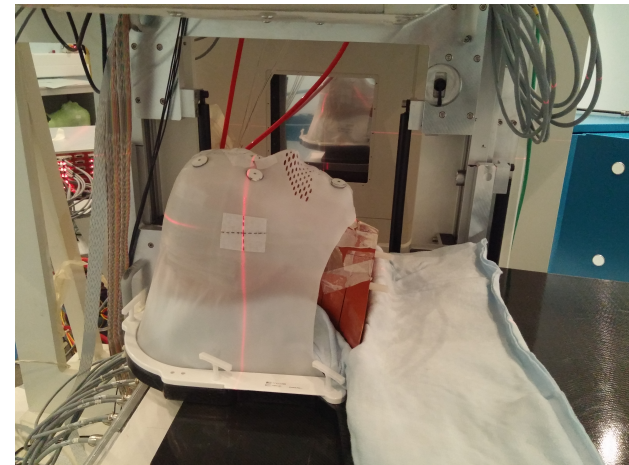
[1] Work partly funded by the European Union 7th Framework Program (FP7/ 2007-2013) under Grant Agreement No. 256984 EndoTOFPET-US and supported by a Marie Curie Early Initial Training Network Fellowship of the European Union 7th Framework Program (PITN-GA-2011-289355-PicoSEC-MCNet).

Commissioning



On-line or off-line 3D PET image reconstruction
Maximum Likelihood Estimation Maximization
(MLEM) iterative algorithm, five iterations
FOV 224 x 112 x 264 mm³
Voxel 1.6x1.6x1.6 mm³

- CNAO test beams
 - Protons, Carbon Ions
 - Pencil beams, Energy layers and Treatment Plans (TP)
 - Energy 60-210 MeV (protons)
- PMMA (w air/bone inserts) and Anthropomorphic phantoms

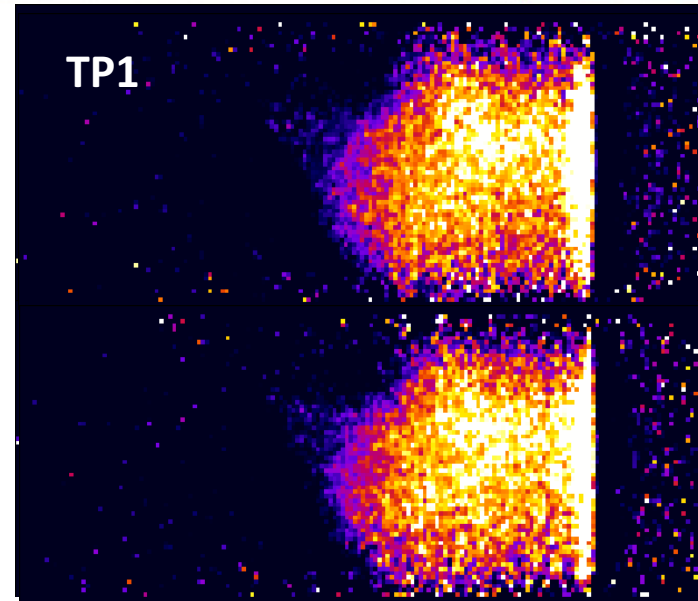


Treatment Plan Delivery

SIMULATION

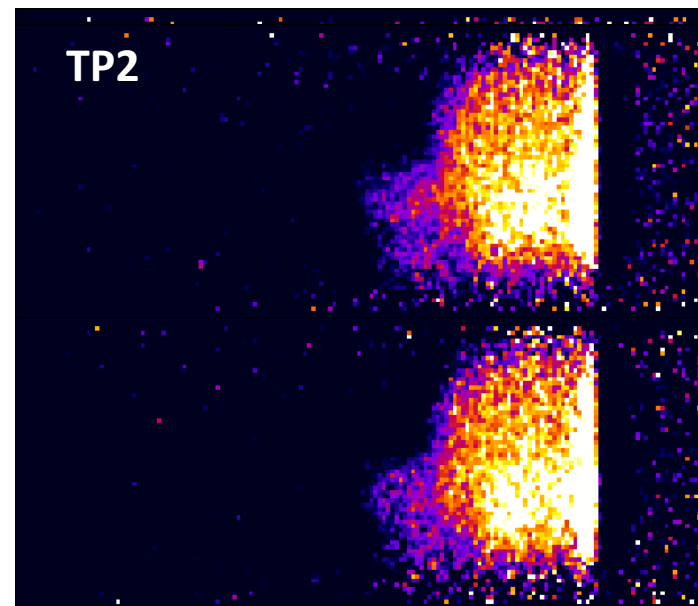
Tool for range comparison between measured and reference (simulated or measured in previous sessions) distributions

	TP1	TP2
Energy range	82-150 MeV	62-129 MeV
Dose	1 Gy	1Gy



MS1

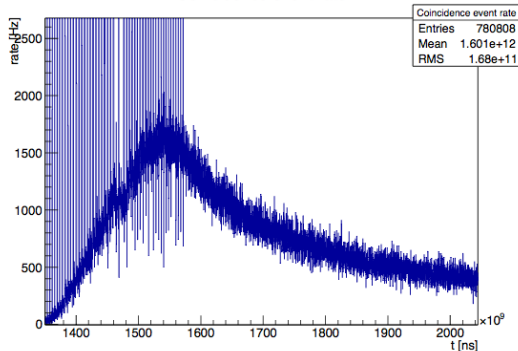
MS2



MS1

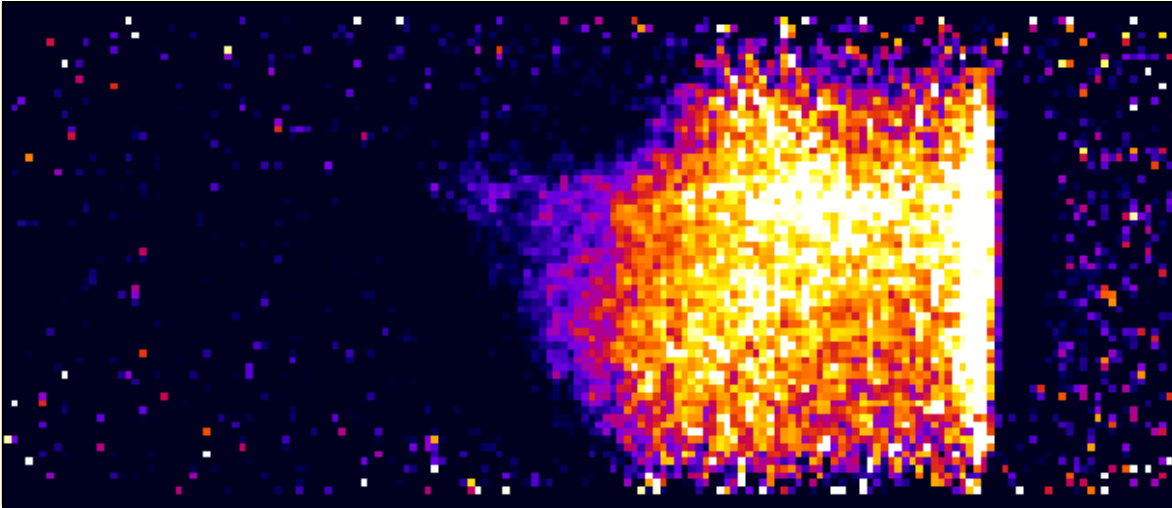
MS2

Coincidence event rate

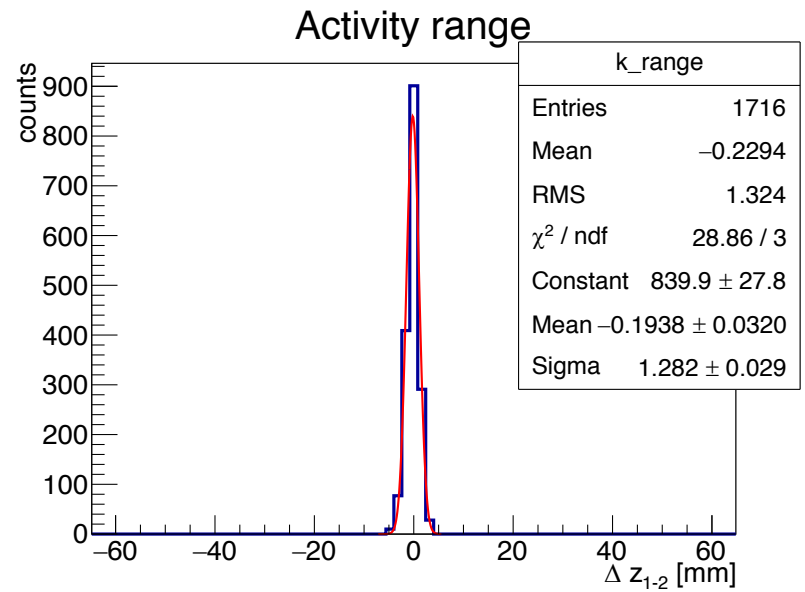


Statistical coincidence event rate and 700 s treatment on+after treatment



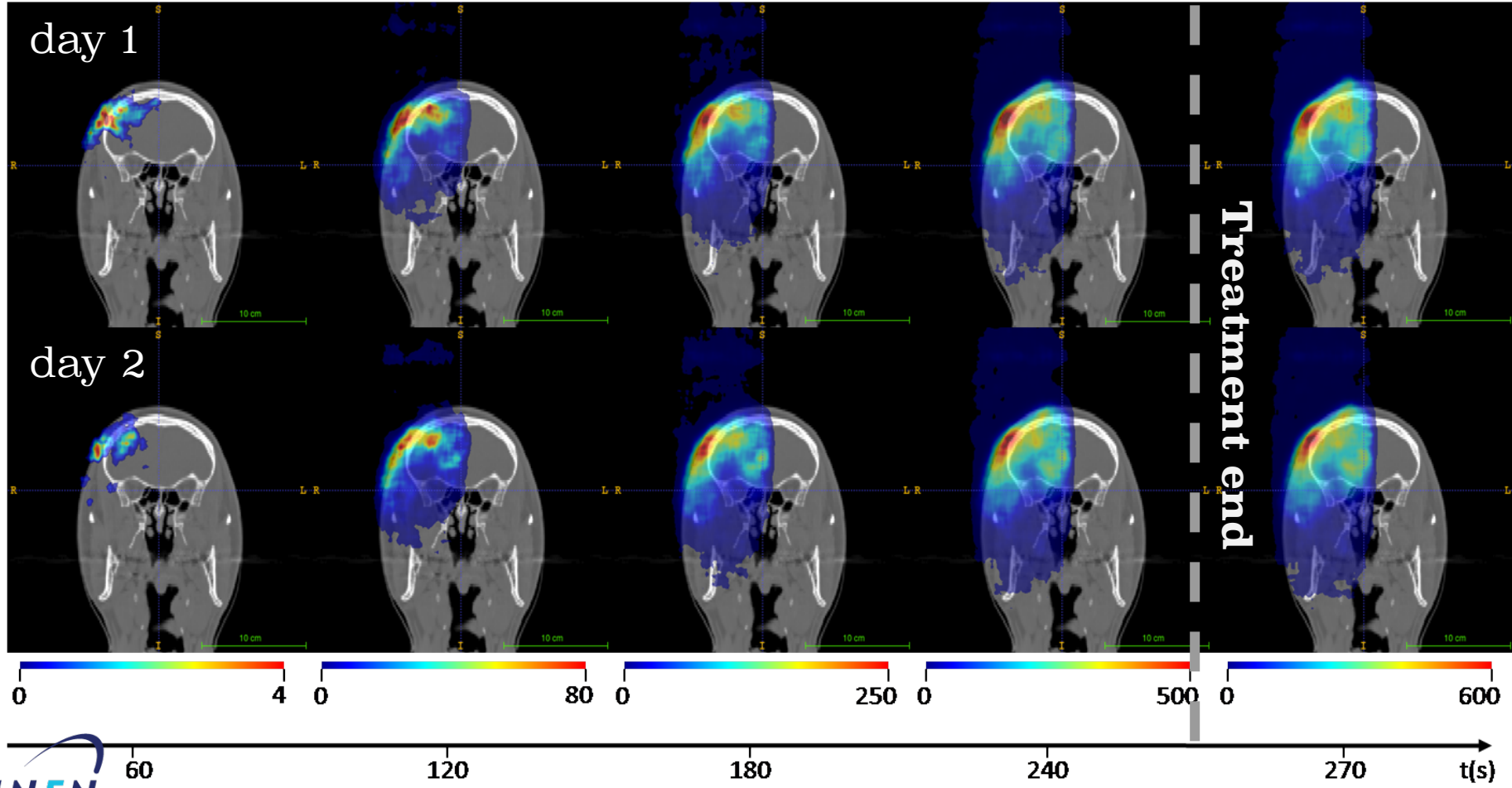


TP1 M1/TP1 M2

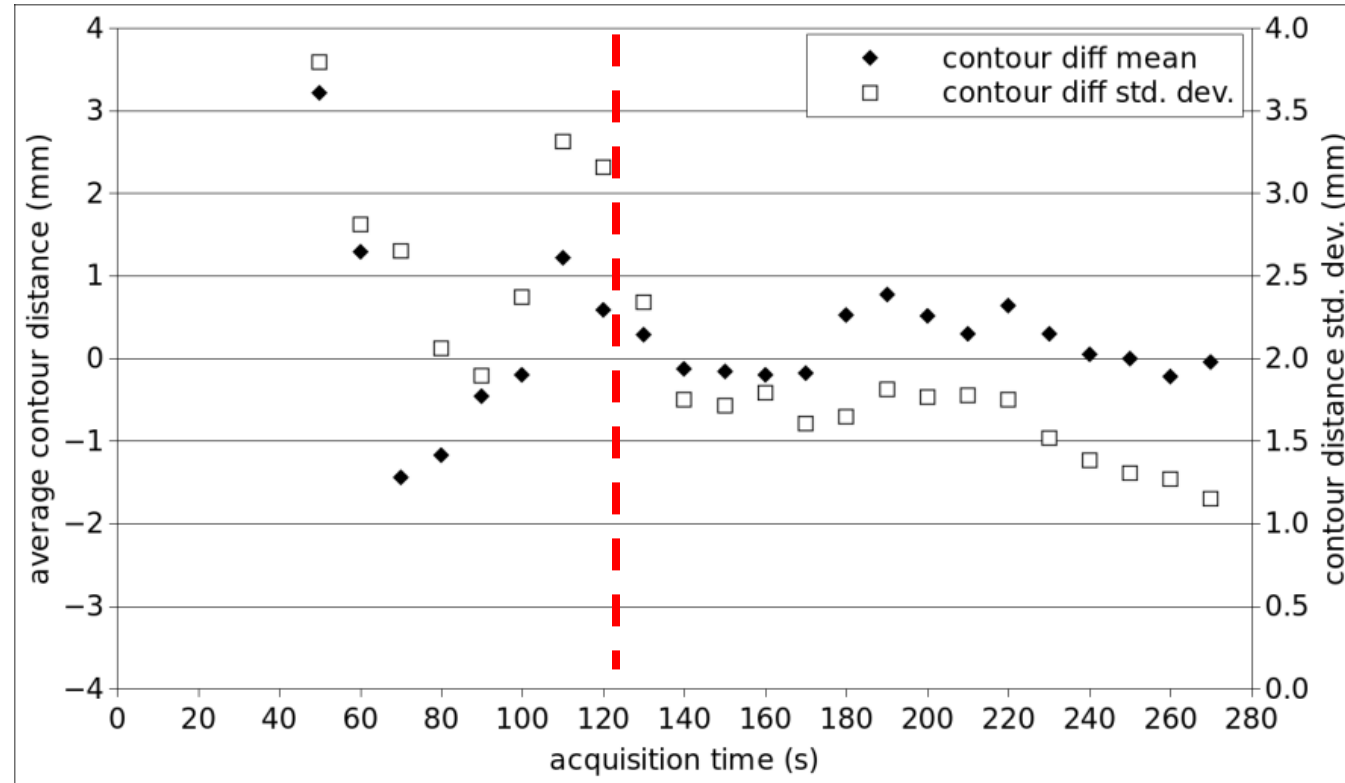
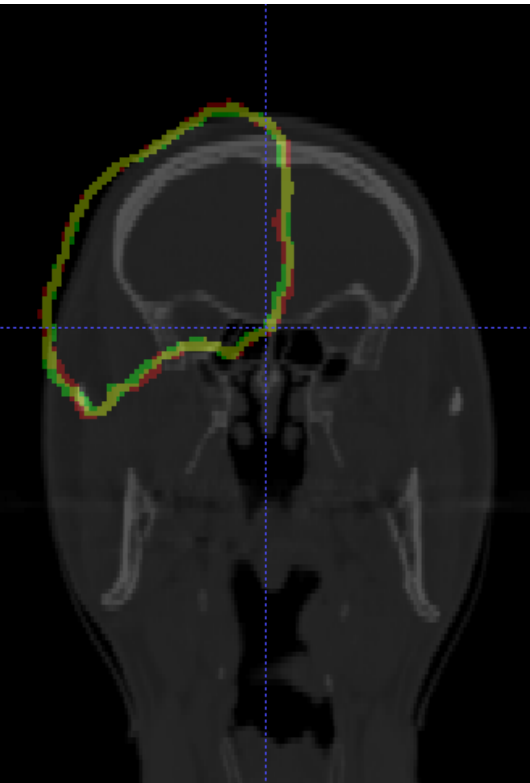


Time-resolved image reconstruction

Measured activity

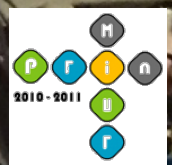
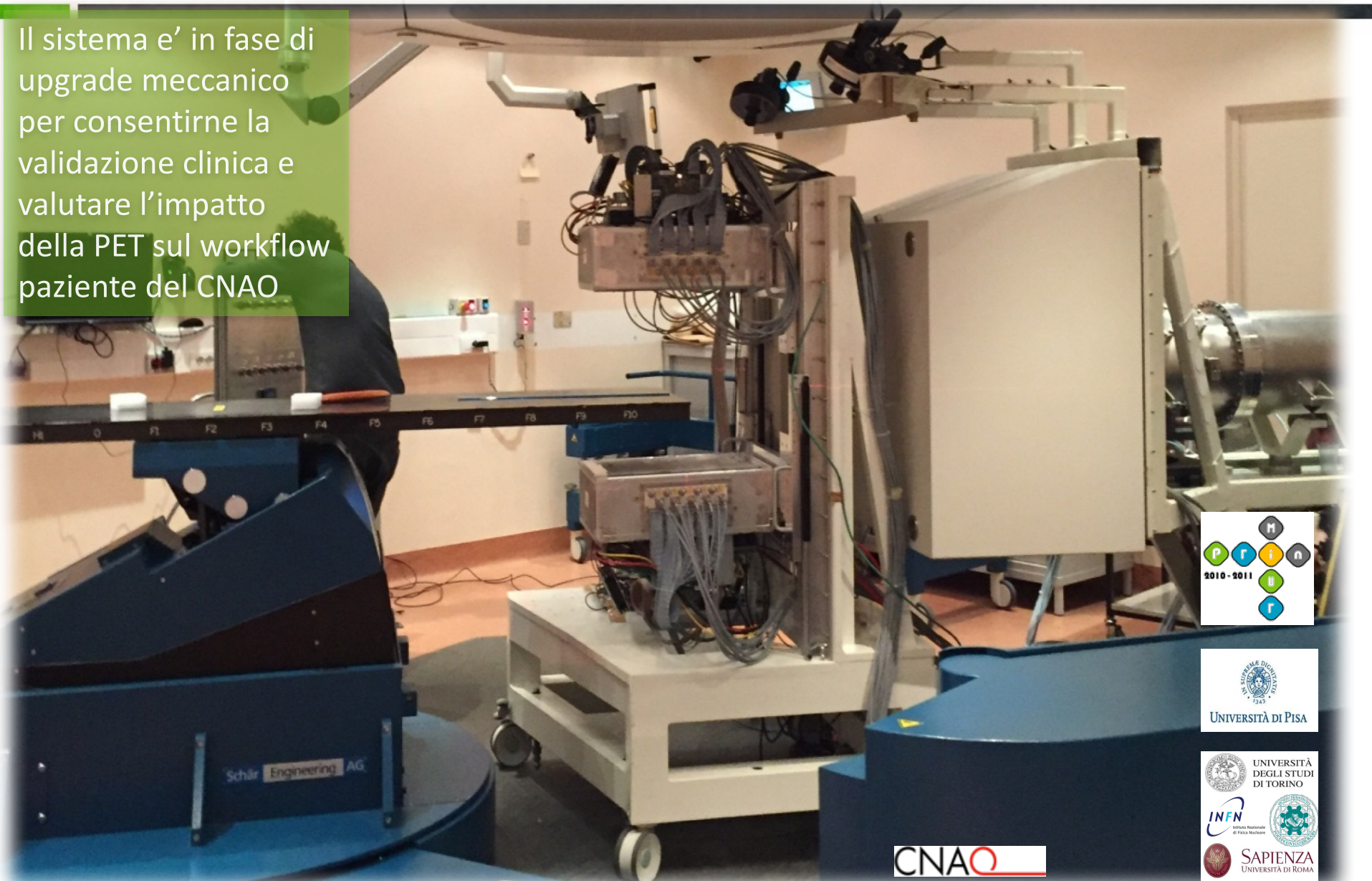


Quantitative comparison



Comparison → after 120 s avg. contour distance < 1 mm

Il sistema e' in fase di upgrade meccanico per consentirne la validazione clinica e valutare l'impatto della PET sul workflow paziente del CNAO





Grazie per l'attenzione!

UOMO virtuale

la fisica esplora il corpo



Pisa, Palazzo Blu
22 marzo – 2 luglio 2017

design Cristina Chiappini

Uomo Virtuale
Pisa, Palazzo Blu, 22 marzo – 2 luglio 2017

Il nostro corpo è un mondo straordinario, che nasconde sorprese ed enigmi, come gli spazi cosmici più remoti o il nucleo infinitamente piccolo della materia.

Abbiamo cominciato a studiarlo fin dall'antichità, per interpretare i sintomi e curare le malattie. Sono state però alcune grandi scoperte della fisica moderna, come i raggi X e la radioattività, a spalancare le porte di quell'universo misterioso, che siamo noi stessi.

Uomo Virtuale racconta l'avventura di questa esplorazione, per cui abbiamo costruito strumenti sempre più potenti: la tomografia computerizzata, la risonanza magnetica, l'ecografia... Veri e propri 'telescopi' e sonde per osservare dentro di noi i dettagli più nascosti degli organi e la trama invisibile della vita. E abbiamo anche inventato nuove tecnologie per curare, come bisturi fatti di particelle per colpire i tumori con sempre maggiore precisione. Fino a sognare, oggi, di potenziare il corpo con organi artificiali e affacciarci a scrutare le connessioni tra i singoli neuroni del nostro cervello. L'uomo virtuale, ricostruito al computer, diventa realtà.

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