Role and challenges of PET imaging in proton therapy

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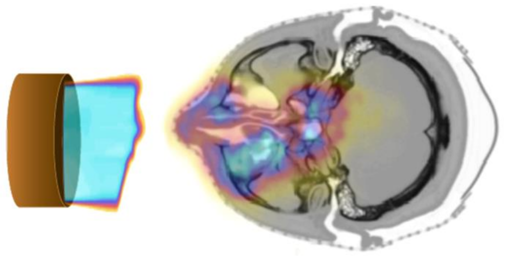
IGFAE: Workshop on technologies and applied research at the future Galician proton-therapy facility

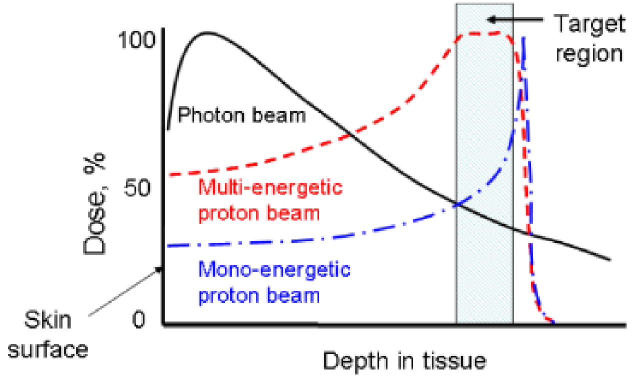
Index

- Introduction
- PET Imaging in ProtonTherapy
- Open Imaging project proposal
- Results
- Conclusions

ProtonTherapy

Proton therapy has the ability to deliver a highly conformal dose to tumors.





https://gordon.mgh.harvard.edu/gc/research/pet-monitoring-of-therapy/

However, proton therapy is also more sensitive to uncertainties in treatment planning and delivery compared to photon therapy.

A range error could mean a portion of a tumor not receiving any radiation dose at all (under-shooting), or the normal tissue lying distal to the beam receiving a full dose (over-shooting).

Proton range inaccuracy is particularly of concern.

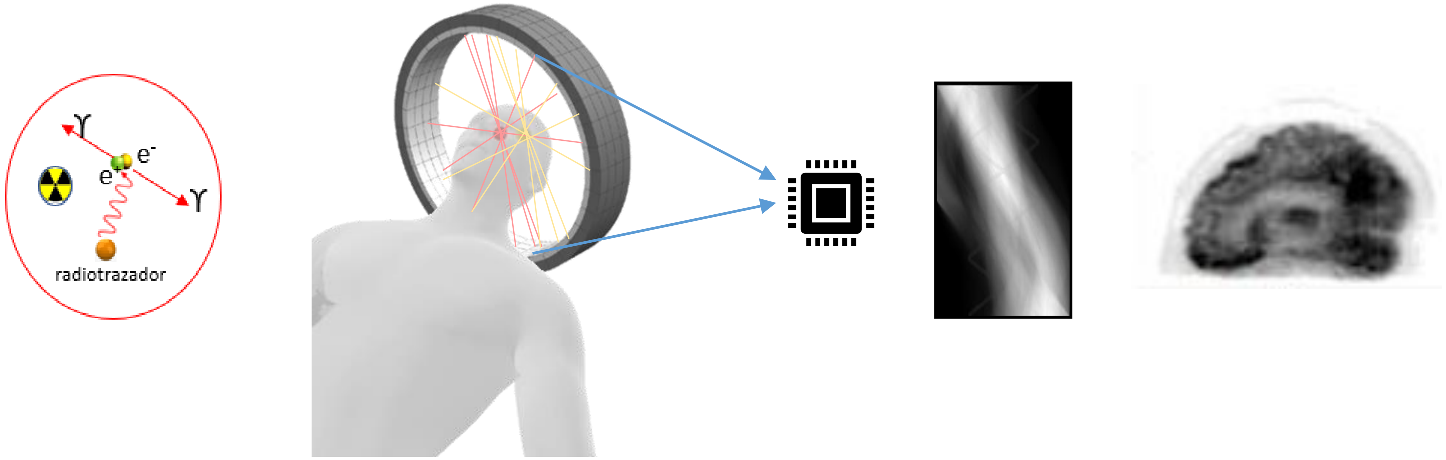
ProtonTherapy

During proton therapy irradiation, **several positron emitters** are produced in the living tissue from the interactions of protons having the main interest ^{11}C and ^{15}O with half-lifes of approximately 20 and 2 min, respectively.

Atom	Reaction	Isotope	$t_{1/2}$ (min)
^{16}O	p,pn	^{15}O	2,037
^{12}C	p,pn	^{11}C	20,39
^{14}N	p, 2p2n	^{11}C	20,39
^{16}O	p, 3p3n	^{11}C	20,39
^{16}O	p, 2p2n	^{13}N	9,965
^{14}N	p,pn	^{13}N	9,965
^{31}P	p,pn	^{30}P	2,498
^{40}Ca	p,2pn	^{38}K	7,636

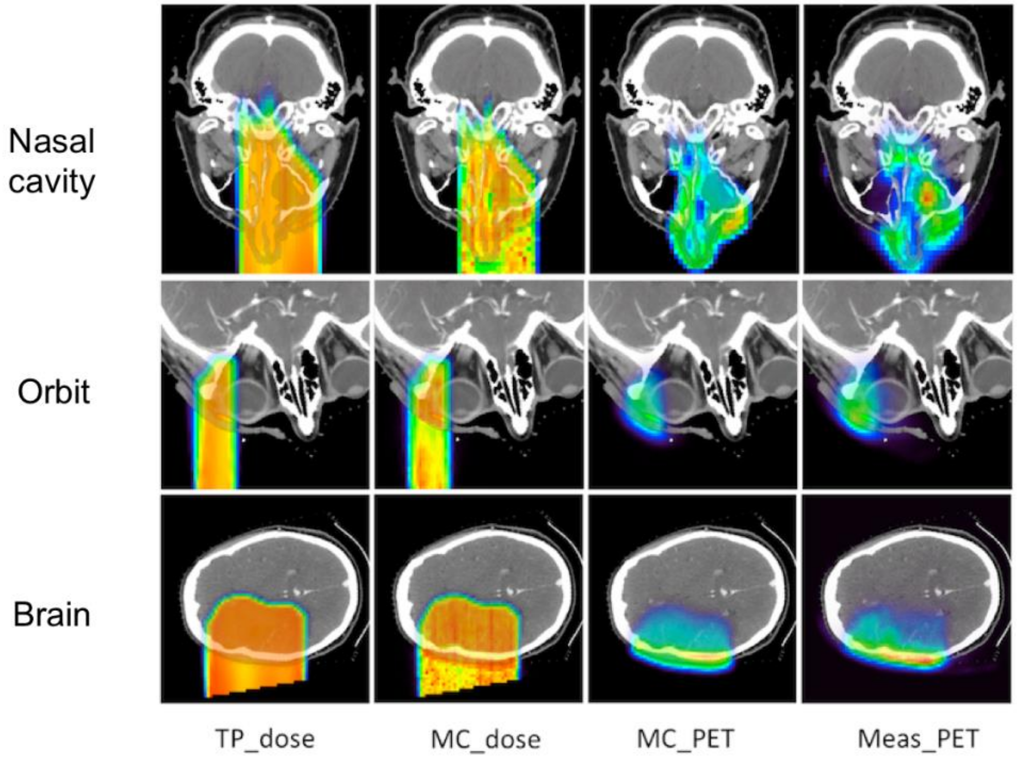
Several positron emitters produced inside the different tissues of the human body when it is irradiated by protons

In therapy, therefore, PET cameras may be used to detect the emitted photons from the positron radioisotopes produced during proton therapy and create an image of the radioactivity generated.



PET in ProtonTherapy

PET images in proton therapy are used to perform range proton verifications.



Chul Hee Min et al., Clinical Application of InRoom Positron Emission Tomography for In Vivo Treatment Monitoring in Proton Radiation Therapy, Int J Radiation Oncol Biol Phys, 86 (1), 2013

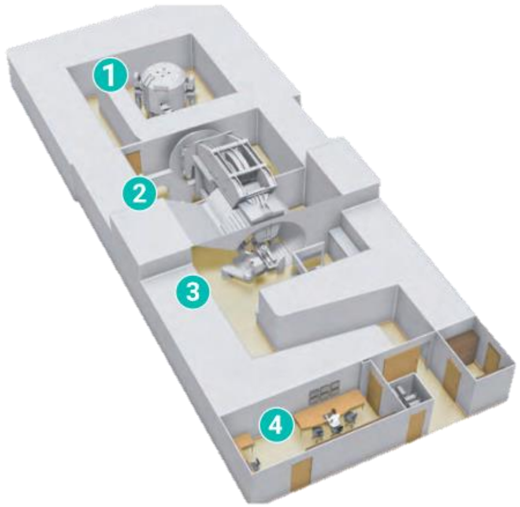
TP_dose: Treatment planned dose
MC_dose: Simulated dose
MC_PET: Simulated PET
Meas_PET: Measured PET

In vivo PET range verification relies on the comparison of measured and simulated activity distributions.

PET in ProtonTherapy

PET images in proton therapy are used to perform range proton verifications: Off-line PET, in-room PET, in beam PET

Off- line PET, usually an established scanner in a nearby location



First center of Spanish proton therapy
(Quiron, Pozuelo de Alarcón)

1. Energy room
2. Proton therapy system
3. Treatment room
4. Control room

- It does not require capital investment.
- Usually includes anatomical information (PET/TC).
- It has no impact on the patient throughput in the treatment room
- Relatively long delay for PET acquisitions. Use of contrast has been proposed to increase the available positron sources generated (*)
- Affected by the biological washout
- Patient repositioning

* España, S., Sánchez-Parcerisa, D., Bragado, P. *et al.* In vivo production of fluorine-18 in a chicken egg tumor model of breast cancer for proton therapy range verification. *Sci Rep* **12**, 7075 (2022). https://doi.org/10.1038/s41598-022-11037-7

PET in ProtonTherapy

In-room PET, positioned within the treatment room

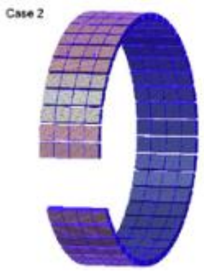
Chul Hee Min et al., Clinical Application of InRoom Positron Emission Tomography for In Vivo Treatment Monitoring in Proton Radiation Therapy, Int J Radiation Oncol Biol Phys, 86 (1), 2013

- ❑ A full-ring detector can be used for complete data.
- ❑ Less delay between treatment and PET scan.
- ❑ Complications caused by biological washout, repositioning errors, anatomical changes, etc., are greatly reduced or eliminated.
- ❑ Has a relatively higher impact to the patient throughput in the treatment room.
- ❑ Complicated co-registration PET images and treatment planning CT scan.
- ❑ Implies cost.

PET in ProtonTherapy

In beam PET, detectors integrated into the beam delivery system

- PET acquisition can be started as soon as treatment stops or in pauses.
- For treatment sessions with multiple fields, a short PET scan can be taken after the delivery of each field.
- The PET activity level in the tissue is at the highest level.
- Effect of biological washout of PET activities is minimized.
- Patient repositioning errors and anatomical morphologic changes are avoided or minimized.
- Complex synchronization of the PET data acquisition with the beam control system.
- Expensive and technically demanding.
- Geometric constrains in a treatment environment. Full ring detector configuration is not feasible



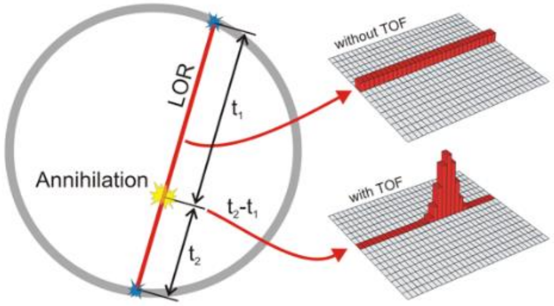
L. Boturra et al. Delivery and Range Monitoring in Particle Therapy in a Higly Innovative Integrated Design, Frontiers in Physics, 8, 2020

Yamaya et al., "An initial investigation of open PET geometries," 2007 IEEE NSSCR, Honolulu, USA, 2007

PET in ProtonTherapy

In beam PET Challenges

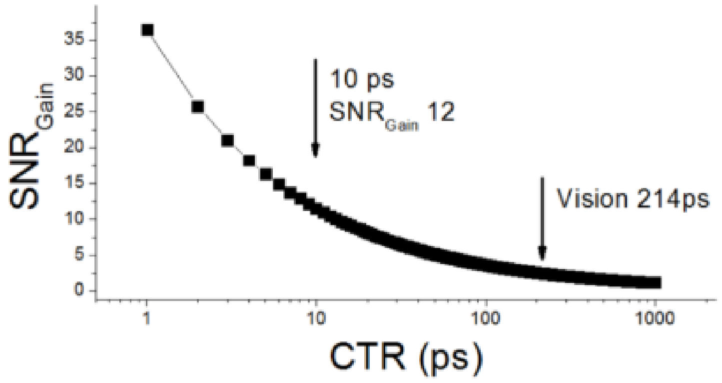
- ❑ Open Geometry
  - ❑ Artifacts.
  - ❑ Low sensitivity .
  - ❑ Image quality, high resolution required for the application.
  - ❑ Limited FOV



https://the10ps-challenge.org/

➢ Current instrumentation developments allows Time of Flight (TOF) providing an useful technique to reduce most of the precedents

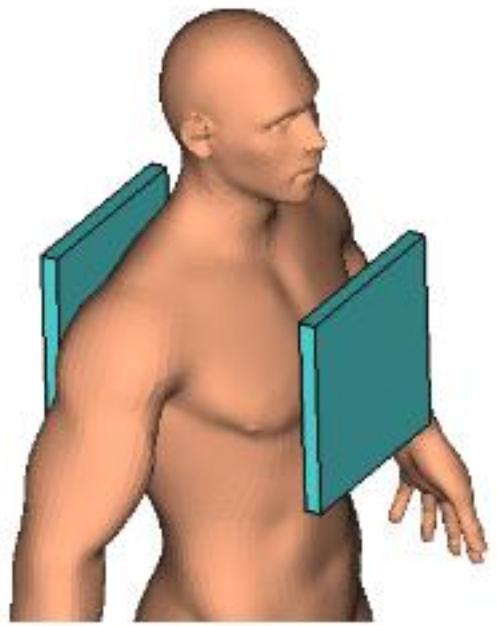
- Reduced artifacts
- Increased SNR with same statistics
- Allow high resolution reconstructions



J. van Sluis et al. "Performance characteristics of the digital Biograph Vision PET/CT system." JNM 60.7, 2019

Open Imaging PET (ERC-2022-POC1, European Commission)

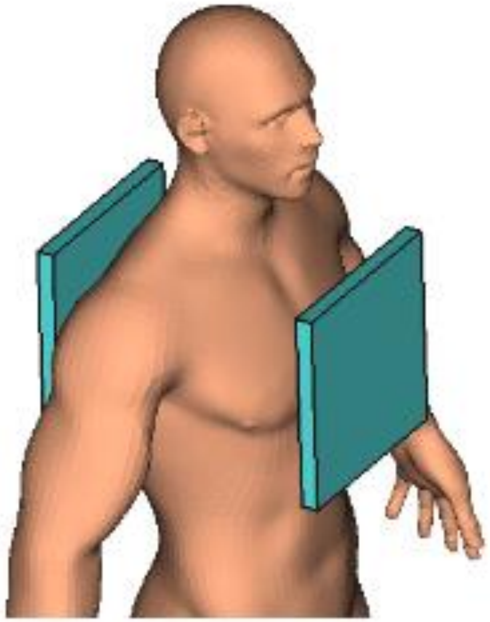
We are developing a proof of concept of a two-paddle PET system, which application is not only focused on therapy, but also on the possibility of using it for radiosurgery and in certain sectors of the population (patients with obesity, claustrophobia or mental illness).

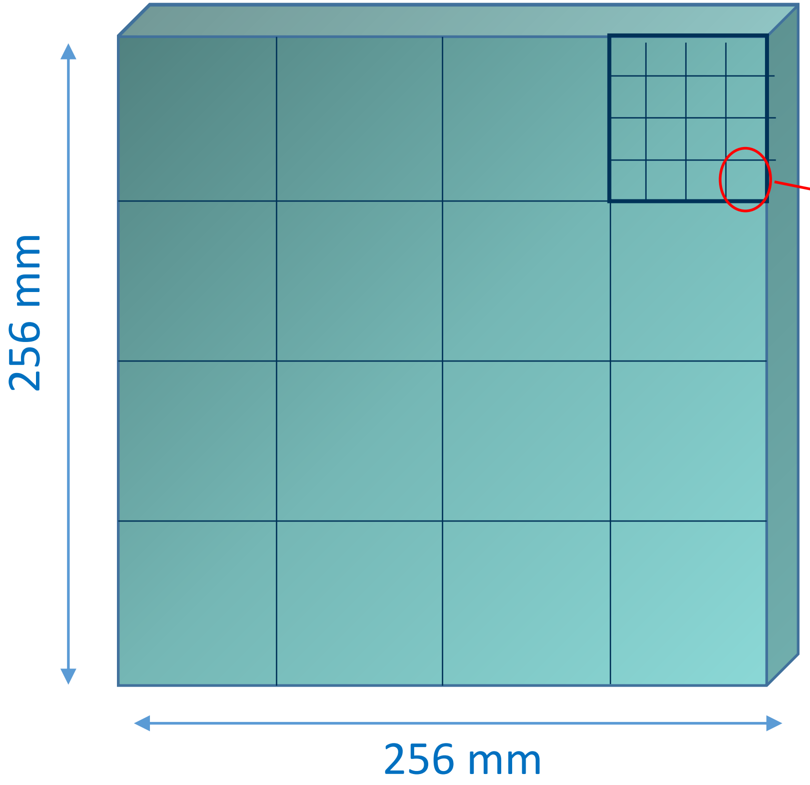


Our proposal is a PET detection system based on two pallets, close to the organ of study, with new detector technology to overcome as possible the limitations of open geometries:

- Large detection surface to maximize sensitivity and allow imaging of any organ.
- High resolution detectors.
- State-of-the-art TOF reducing open geometry artifacts and increasing SNR.

Open Imaging PET (ERC-2022-POC1, European Commission)





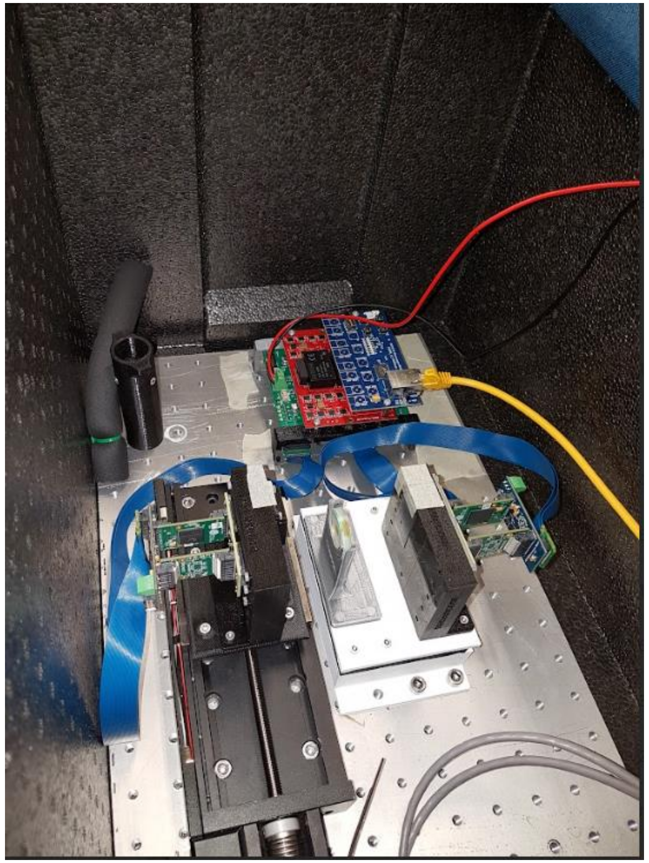
4x4 SUPERMODULES
($64x64mm^2$)

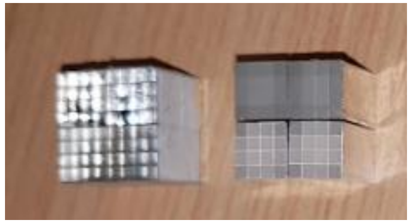
Total: 32768 crystals

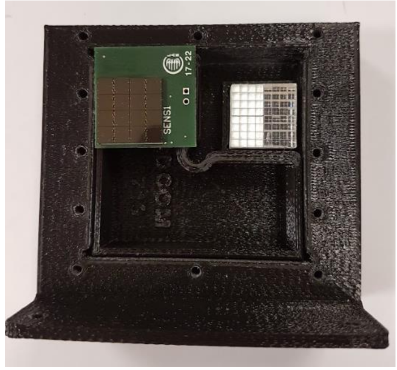
4 x 4 MODULES

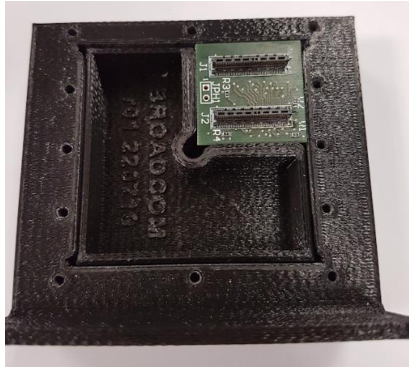
8x8 LYSO crystals $2x2x12\ mm^3$
coupled to a 4x4 array of SiPM of $4x4\ mm^2$

Open Imaging PET (ERC-2022-POC1, European Commission)









- In order to have a cost-effective system the device will use row & column readout for each *supermodule*, reducing from 4096 to 512 channels for each pallet.
- SiPM photodetectors, reducing electronic noise, allowing to work in room temperatures without liquid cooling.
- On-module digitalization to increase temporal resolution accessing the information as soon it is available.
- The digitalization is performed using the TOFPET2 ASIC from PETSys Electronics.

Open Imaging PET (ERC-2022-POC1, European Commission)

The system has been simulated to evaluate the performance using GATE and different TOF resolutions using a distance between pallets of 280mm.

Two reconstruction approaches:

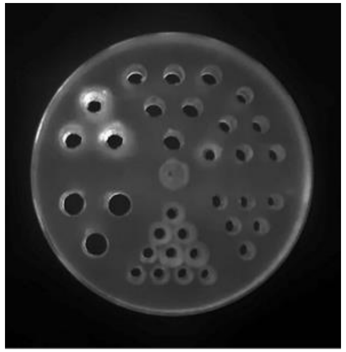
- MLEM using TOF bins
- LMEM TOF

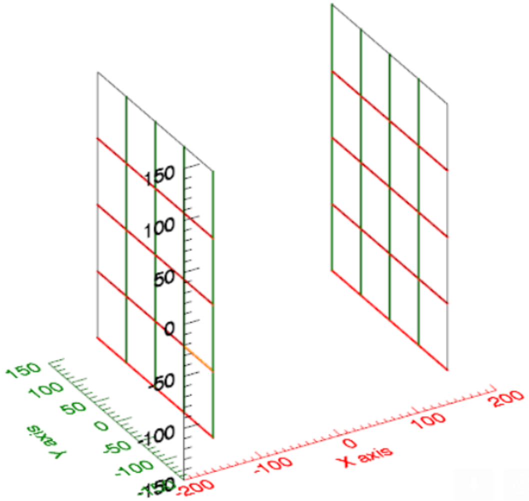
Phantoms:

- NEMA NU-2008 Image Quality
- Derenzo Phantom

Simulation data:

- ^{11}C and ^{15}O as positron emitters.
- Back-to-back.
- 2mm pixel size.





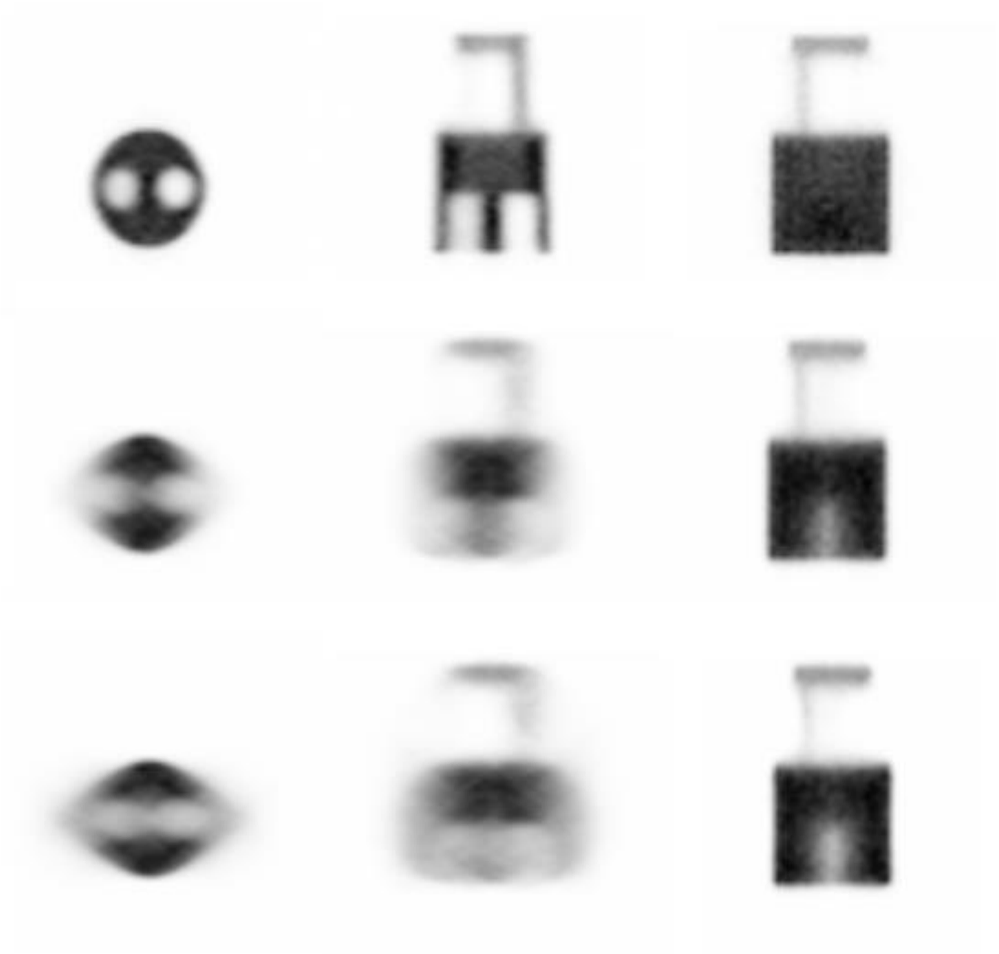
Simulation Results

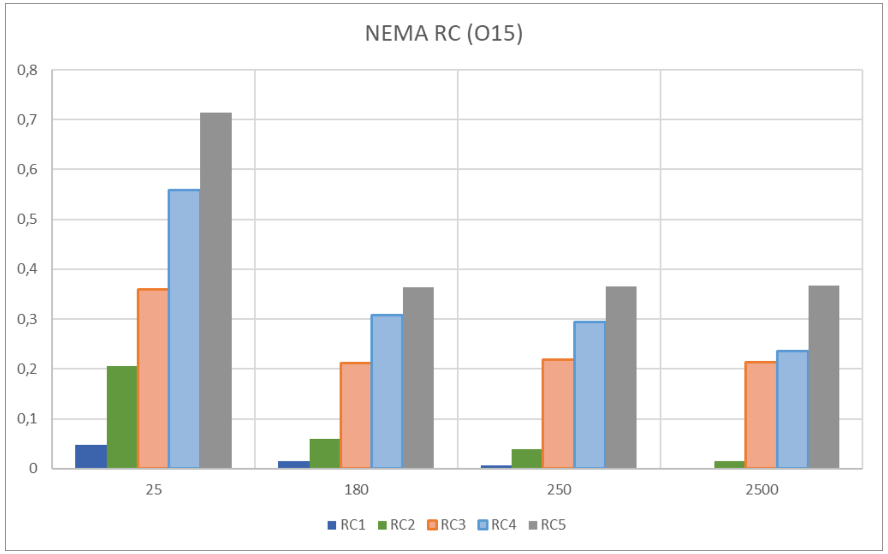
NEMA NU2008 IQ Phantom. ListMode reconstructions (TOR projector, 10 iterations, 2mm pixel size, 1mm voxel size)

25ps

180ps

Non-TOF





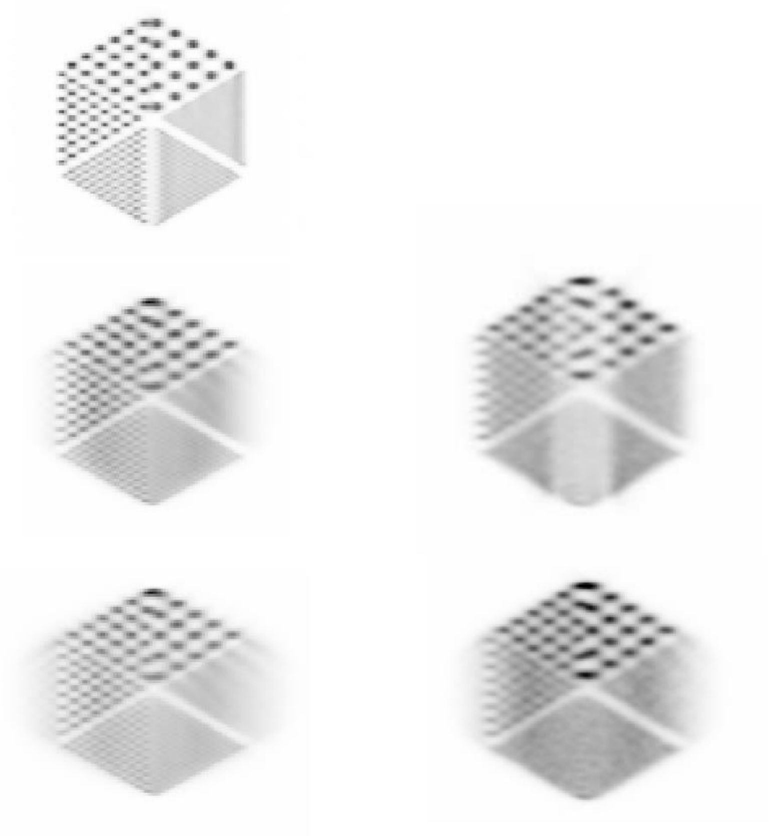
Simulation Results

Derenzo Phantom (rod sizes 1.0, 1.2, 1.6, 2.4, 3.2, 4.0 mm).
Binned TOF reconstructions (MLEM solid-angle projector, 20 iterations, 2mm pixel size, 1mm voxel size).
ListMode reconstructions (TOR projector, 10 iterations, 2mm pixel size, 1mm voxel size).

25ps

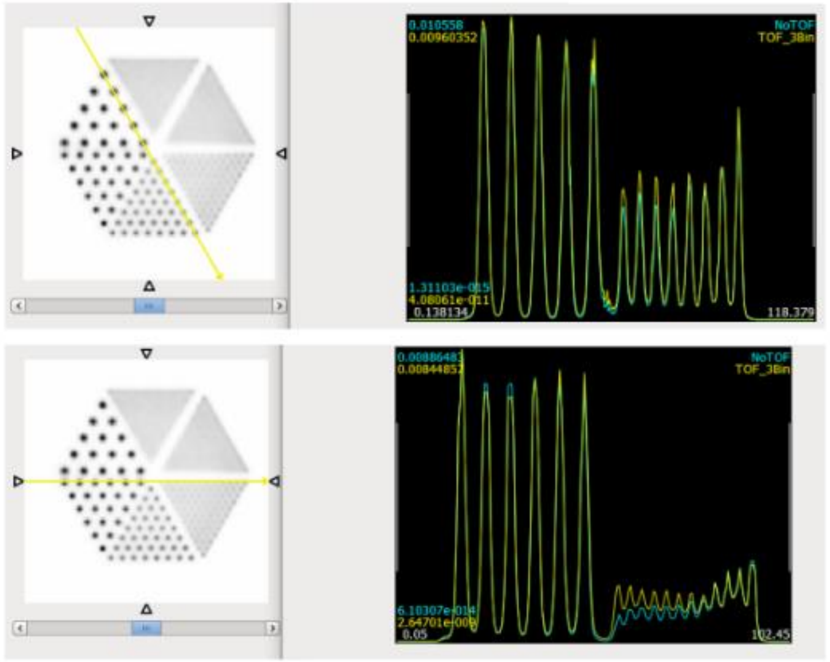
180ps

Non-TOF



LM MLEM

Radial Direction



Conclusions

- The use of PET imaging for range verification in proton therapy requires a very demanding instrumentation.
- Each PET imaging option (in-beam, in-room and off-line) has several advantages and disadvantages
- The most important disadvantage for in-beam PET is the need of open geometries, but this limitation can be partially overcomed using time-of-flight devices, which are currently undergoing a high research activity, reaching about 200ps in commercial systems.
- The Open Imaging Project is building a PET prototype based on two large pallets and time of flight capabilities, which is expected to have an spatial resolution of ~1.5mm and a TOF resolution of 180ps. Using this resolution the expected PET images will be suitable for in-beam PET imaging for range validation in the ProtonTherapy applications

Thanks for your attention

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