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Plan de Recuperación, Transformación y Resiliencia
GENERALITAT VALENCIANA Conselleria de Educación, Universidades y Empleo
GVANEXT Fondos Next Generation en la Comunitat Valenciana

ASFAE ASTROFÍSICA Y FÍSICA DE ALTAS ENERGÍAS

Instrumentation for medical applications

Gabriela Llosá[1]

[1]Instituto de Física Corpuscular (IFIC, CSIC-UV)

Marzo 2024, Alicante

VNIVERSITAT DE VALÈNCIA · UNIVERSITAT POLITÈCNICA DE VALÈNCIA · UNIVERSITAS Miguel Hernández · Universitat d'Alacant Universidad de Alicante · CSIC Consejo Superior de Investigaciones Científicas

Outline

- Challenges in medical imaging instrumentation
  - PET
  - SPECT
  - CT
- Hadron therapy monitoring
- Other

The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Medical imaging

Discovery of X-rays: W. C. Röntgen, 1895.

→ First Nobel Prize in physics, 1901.

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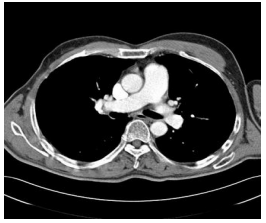
Medical imaging

Structural

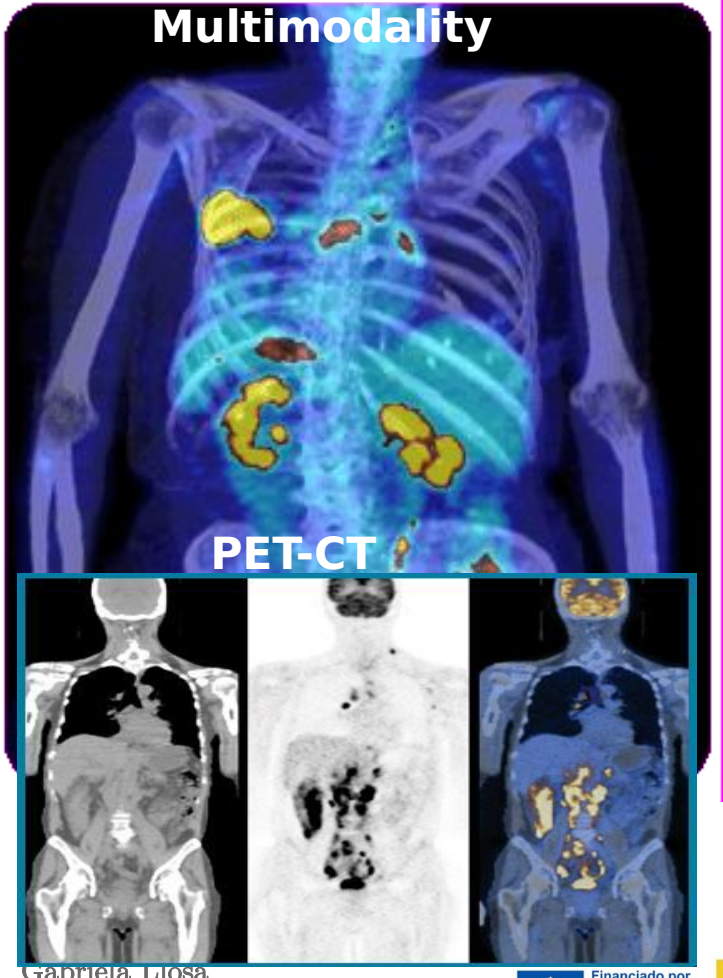
CT



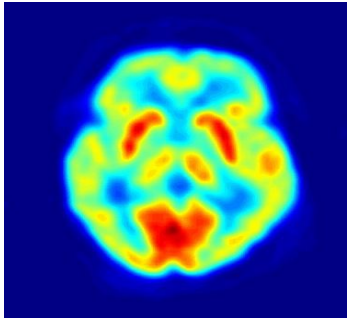
MRI

Ultrasounds

Multimodality



Functional



PET

SPECT

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Goals

- Improve diagnostic accuracy
- Reduce dose / time

  + Lower cost

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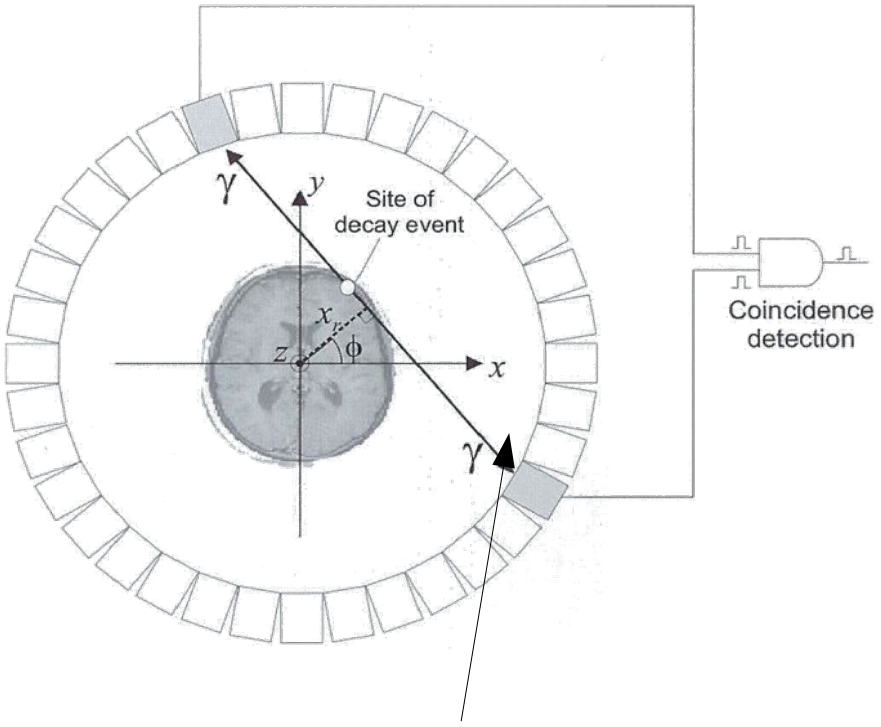
Positron Emission Tomography (PET)

Ring of detector heads



Line of response (LOR)

- Positron emitters
- 511 keV photons
- Most common radiotracer: ^{18}F-FDG

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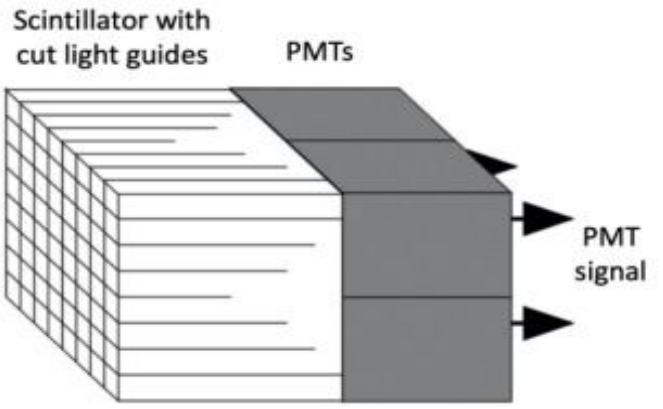
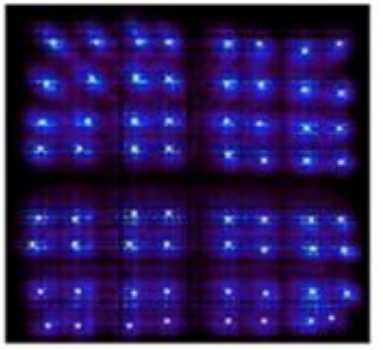
PET - detectors

Block detector: BGO + PMTs.
4-6 mm crystal size

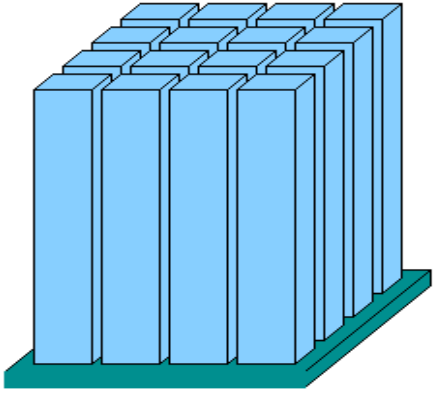




LSO / LYSO + SiPMs. 3-4 mm crystal size

One-to-one coupling or Multiplexing solutions to reduce the number of channels

(→ PET/MR)



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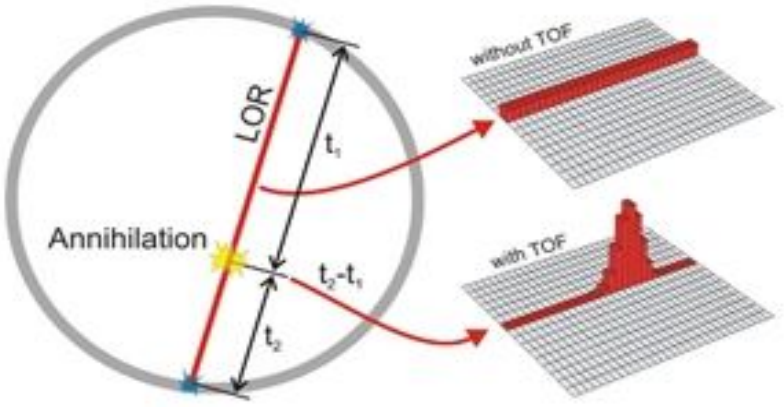
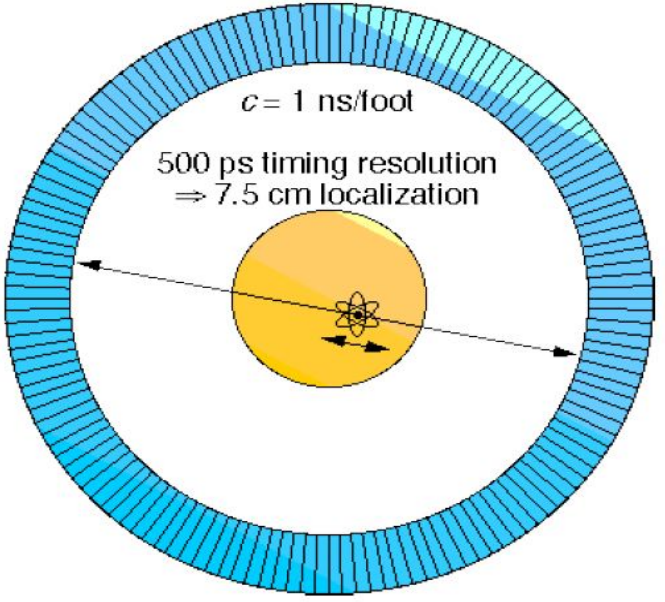
Time-Of-Flight (TOF) PET

$$\Delta d = \Delta t \times \frac{c}{2}$$





More accurate determination of the emission area of the photons
→ better signal-to-noise ratio (SNR).

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TOF-PET first generation

- PHILIPS Gemini TF: LYSO ~550 ps FWHM
- Siemens Biograph mCT: LSO ~529 ps FWHM

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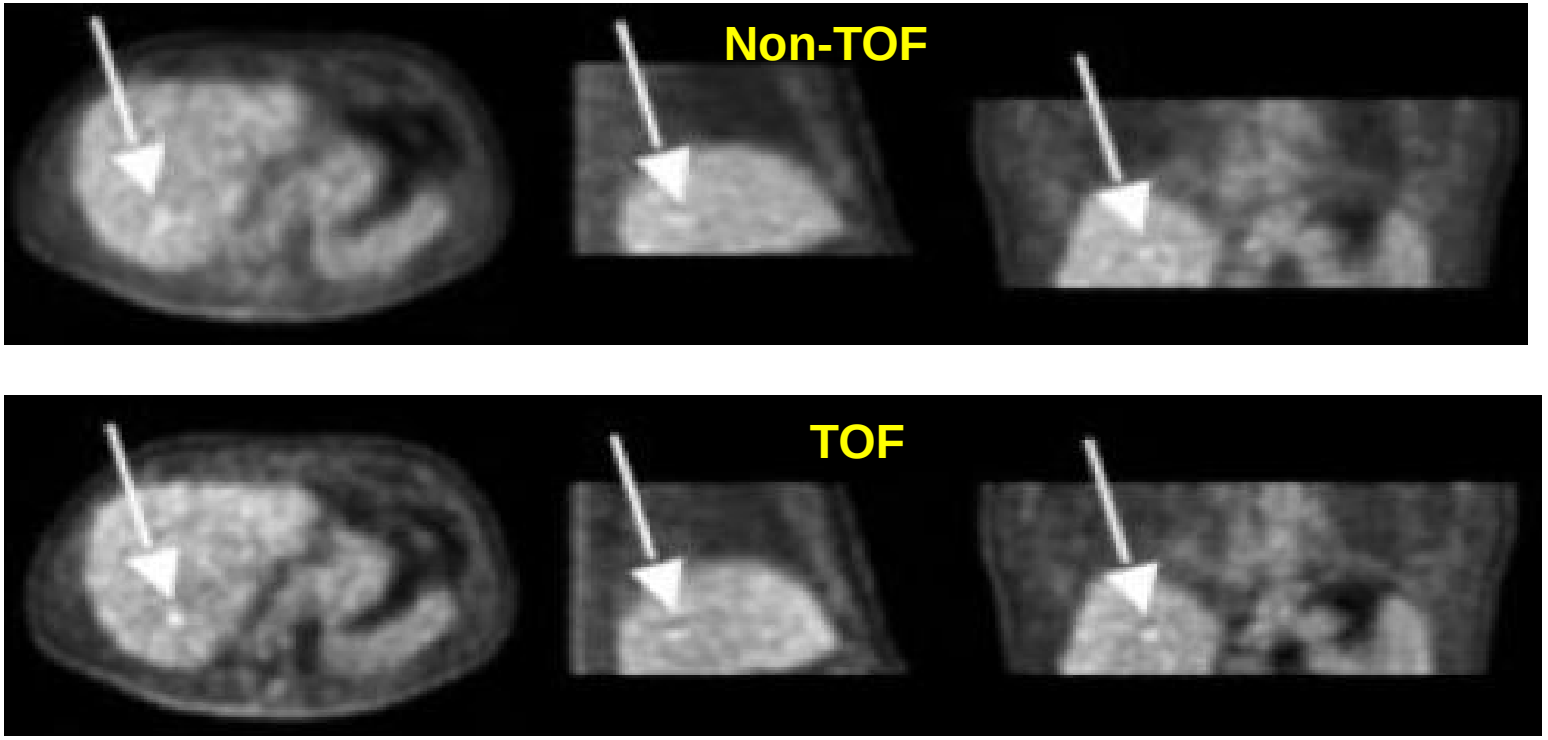
TOF-PET



Liver lesion

Surti et al.
J Nucl Med 52(5). 2011

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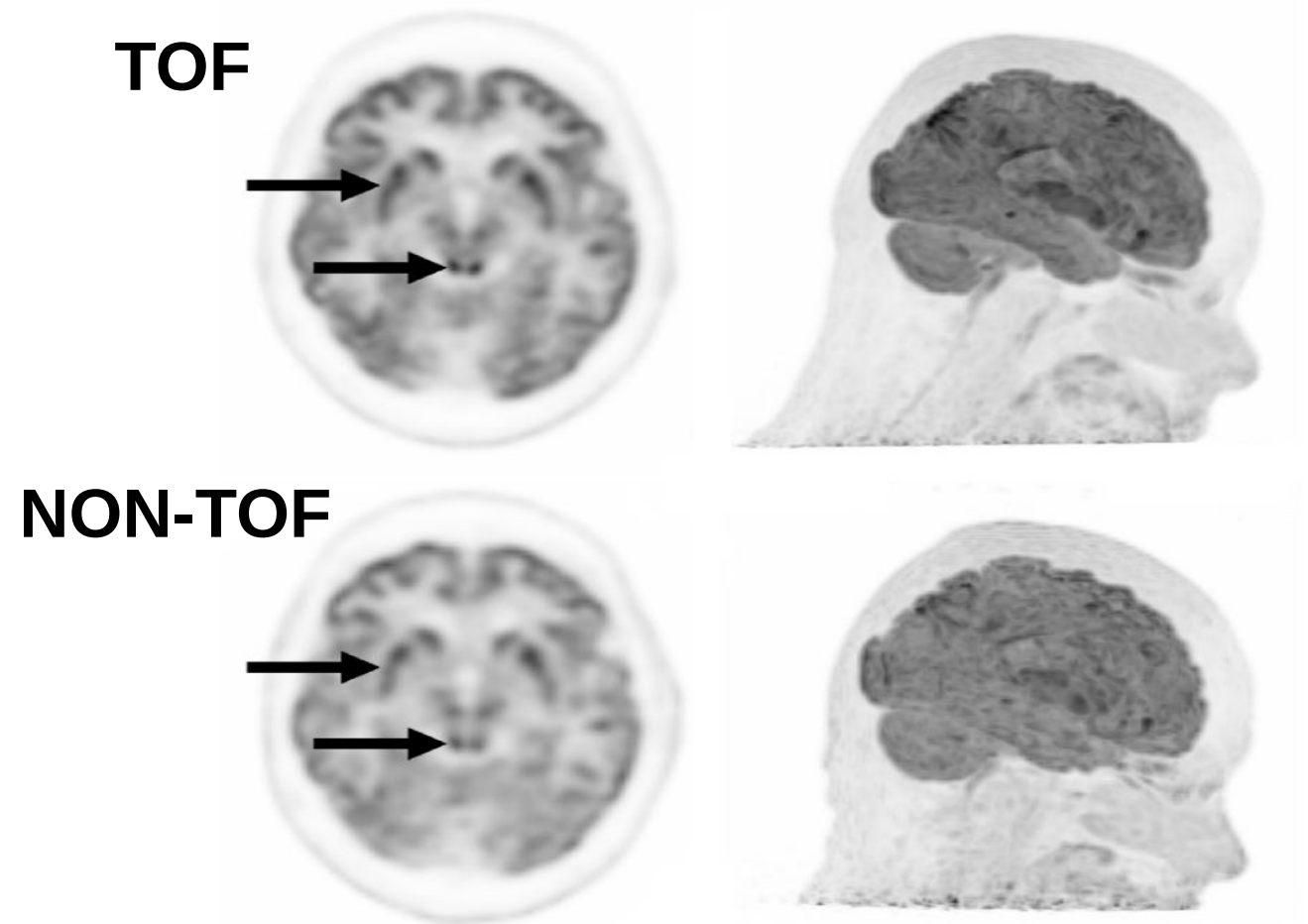
TOF-PET



Van Sluis et al.

J Nuc Med 2019

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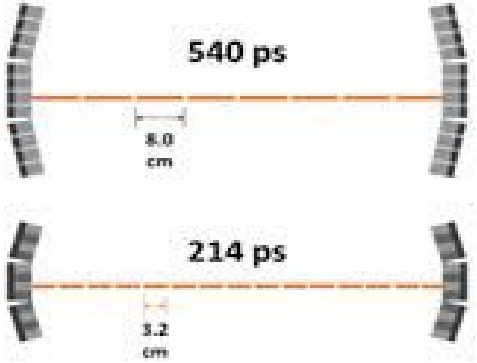
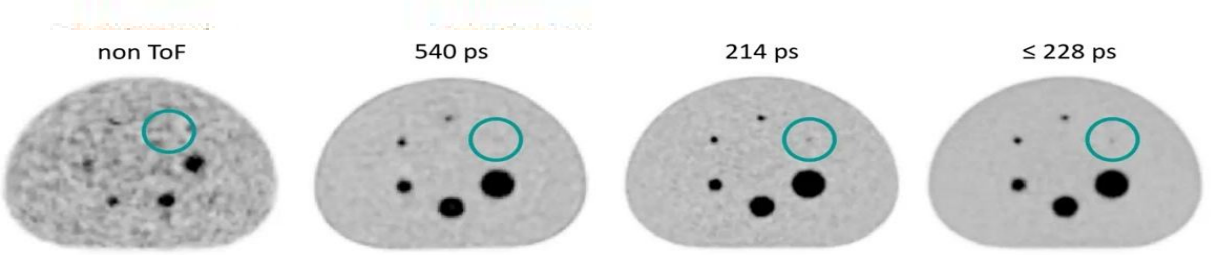
TOF-PET

Last generation with SiPMs: 214-380 ps FWHM





Sphere size (mm): 5, 8, 10, 13, 28, 37; 4:1 CBR

Siemens Biograph Vision: 214 ps.

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TOF-PET

The 10 ps challenge → 1.5 mm LOR

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Physics in Medicine & Biology

ROADMAP

Roadmap toward the 10 ps time-of-flight PET challenge

Paul Lecoq[1], Christian Morel[2], John O Prior[3], Dimitris Visvikis[4], Stefan Gundacker[1,5], Etiennette Auffray[1], Peter Križan[6], Rosana Martinez Turtos[1,21], Dominique Thers[7], Edoardo Charbon[8], Joao Varela[9], Christophe de La Taille[10], Angelo Rivetti[11], Dominique Breton[12], Jean-François Pratte[13], Johan Nuyts[14], Suleman Surti[15], Stefaan Vandenberghe[16], Paul Marsden[17], Katia Parodi[18], Jose Maria Benlloch[19] and Mathieu Benoit[20] – Hide full author list

Published 20 October 2020 • © 2020 Institute of Physics and Engineering in Medicine
Physics in Medicine & Biology, Volume 65, Number 21
Citation Paul Lecoq *et al* 2020 *Phys. Med. Biol.* **65** 21RM01
DOI 10.1088/1361-6560/ab9500

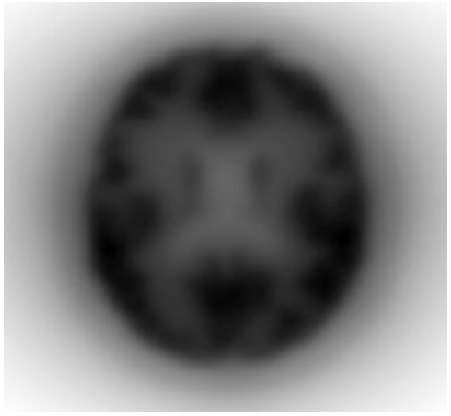
+ Article and author information

Abstract

Abstract

Since the seventies, positron emission tomography (PET) has become an invaluable medical molecular imaging modality with an unprecedented sensitivity at the picomolar level, especially for cancer diagnosis and the monitoring of its response to therapy. More recently, its combination with x-ray computed tomography (CT) or magnetic resonance (MR) has added high precision anatomic

Non-TOF



TOF 10 ps

unlikely that a CTR of 100 ps or better can be reached with standard scintillator technology

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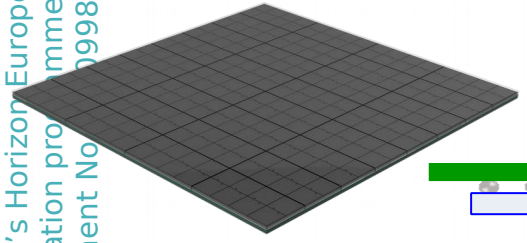
Next generation limited-angle time-of-flight PET imager

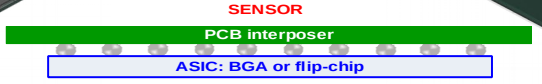
http://petvision.org

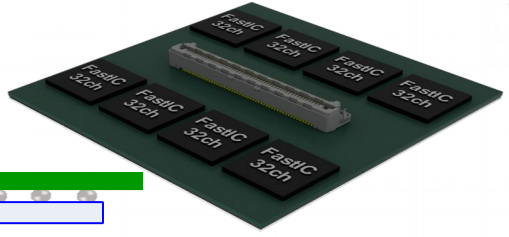
Funded by the European Union

This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101099896

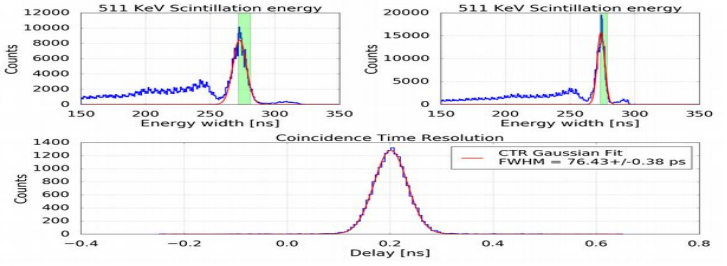
Explore the ultimate time resolution (<80 ps CTR) by integrating photo sensor and the FastIC readout





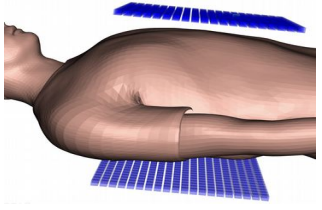


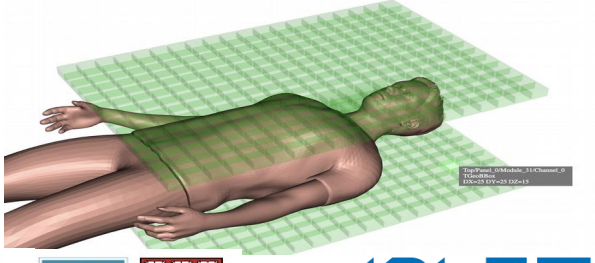
Preliminary results (non-integ. sensor)



FastIC+ FBK NUV-HD + 2x2x3mm3 LSO FWHM = 76 ps

Enable limited angle and affordable total body devices





Courtesy of Rok Pestotnik

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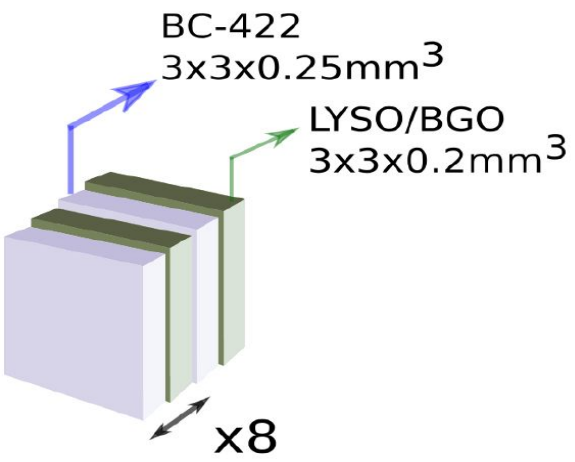
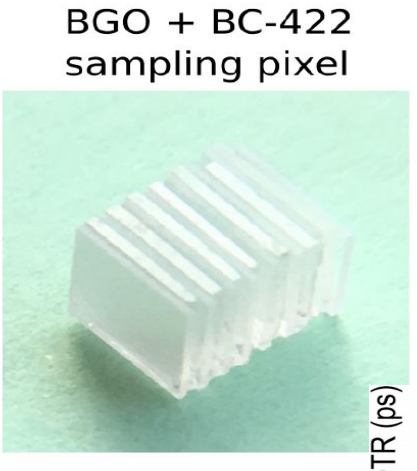
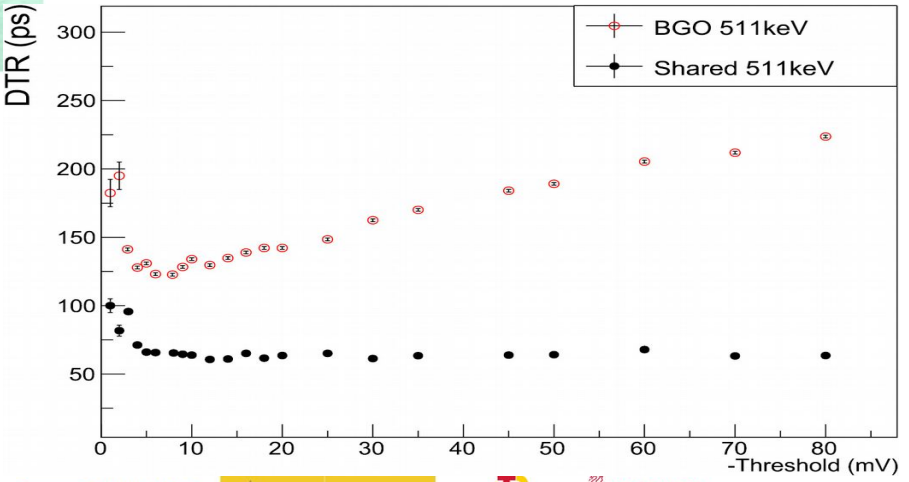
TOF-PET

New materials / metamaterials.





R M Turtos et al. Phys. Med. Biol. 2019



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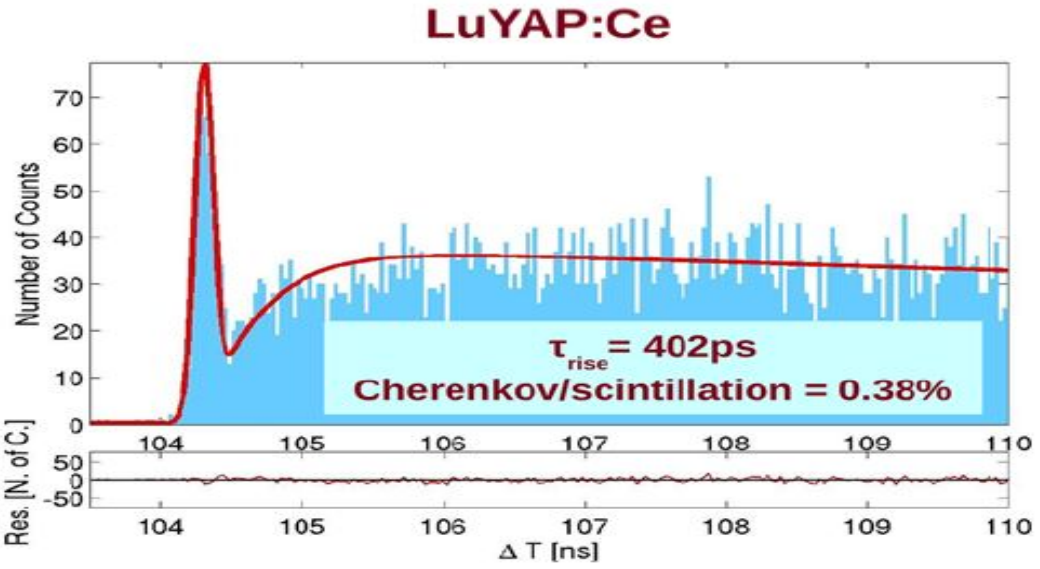
TOF-PET

Prompt / Cherenkov photons in scintillator crystals.



S. Gundacker et al. Phys. Med. Biol. 61 (2016)

BGO could be a promising scintillator for this application

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Cherenkov PET

- PbF_2 + MCP PMTs
- 511 keV photons produce

  ~ 10 Cherenkov photons.
- Measured timing resolution: 84.6 ps FWHM.
- Tests with cooled SiPMs.

S. Korpar et al. Physics Procedia 37 (2012)

S. Korpar et al. / Physics Procedia 37 (2012) 1531 – 1536

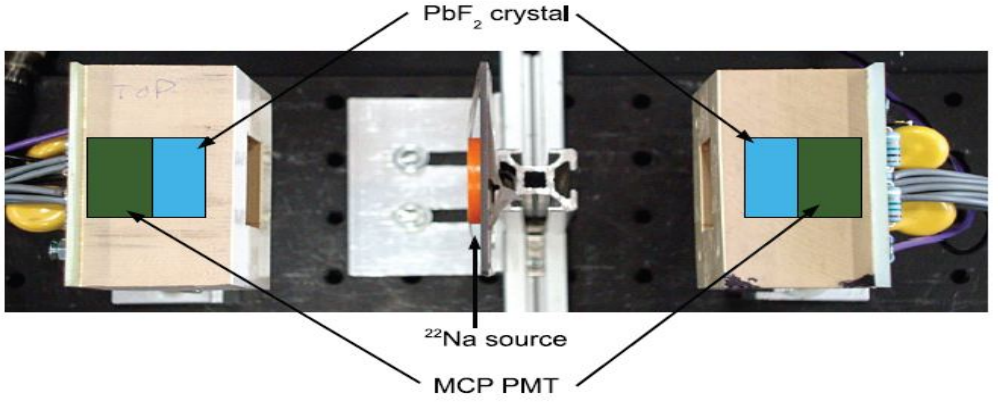

Fig. 1. The experimental setup with ^{22}Na source in between the two PbF_2 crystals coupled to MCP PMTs.

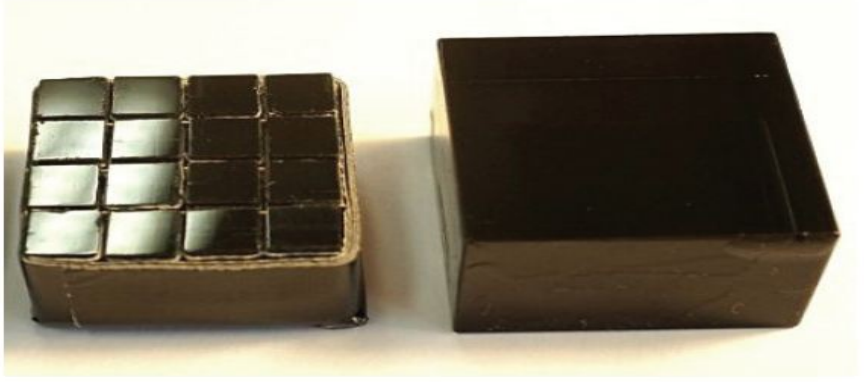

Fig. 2. Cherenkov radiator crystals used for detection of 511 keV photons in the present experiment.

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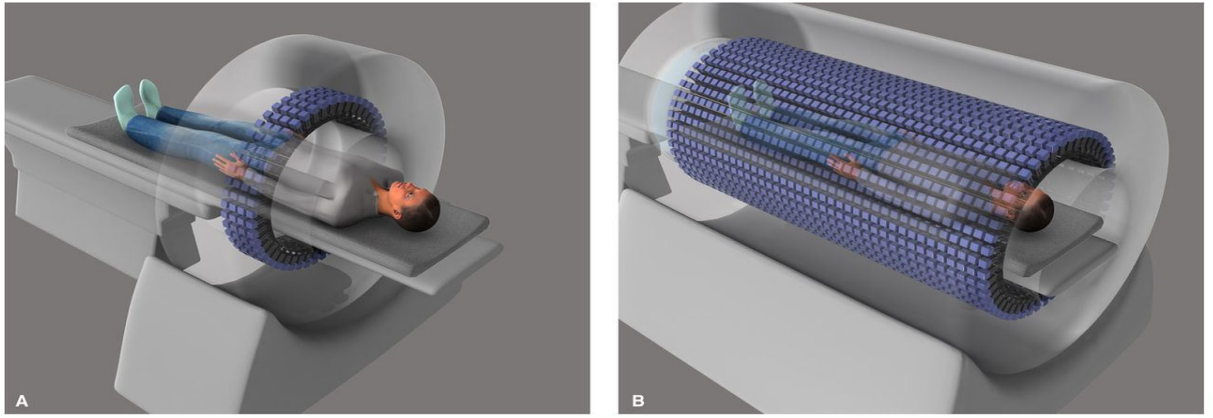
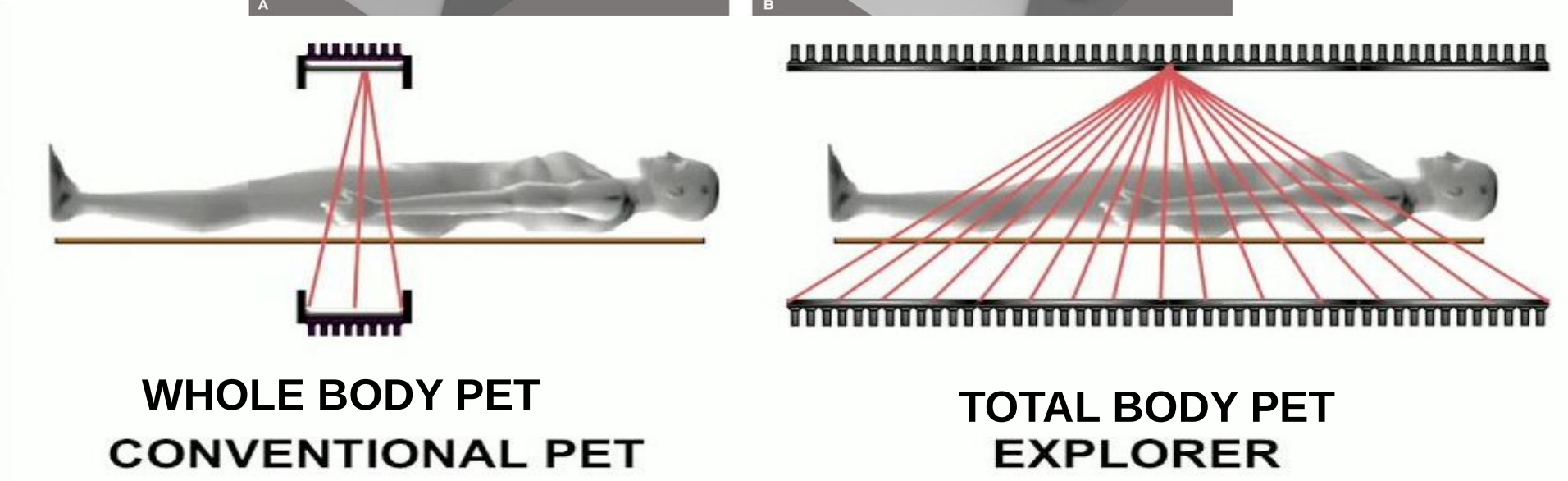
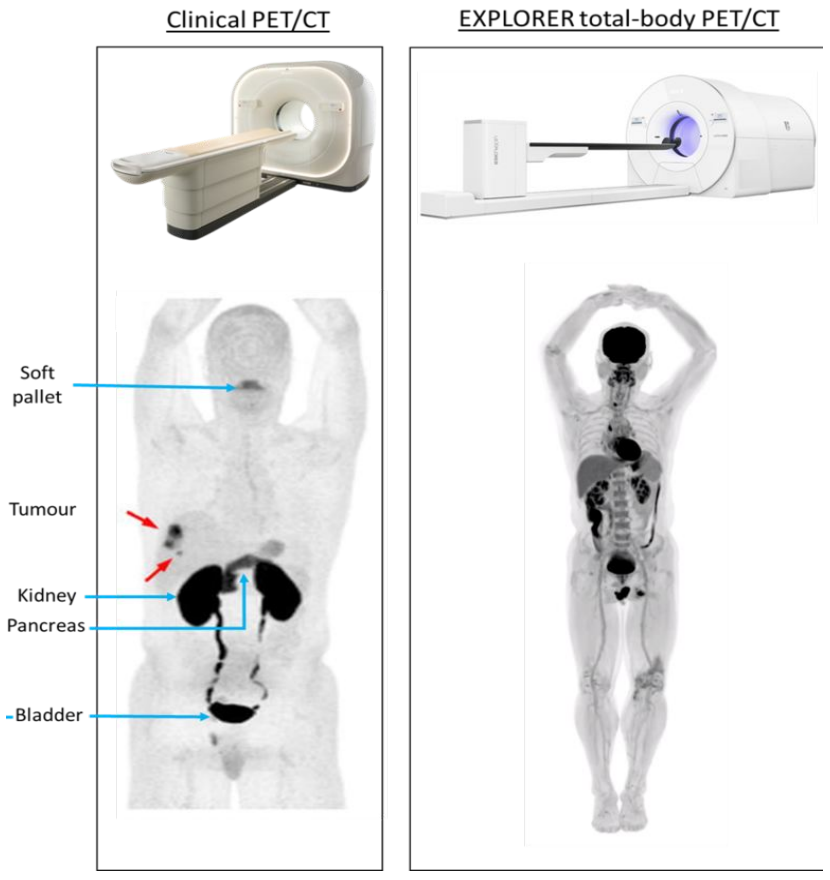
Total Body PET





The ASI
MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Total Body PET



- Sensitivity 40x: faster images or lower dose

  → repetition of scans, pediatric scans…

- Image of the whole body in 20-30 s.

- Large FOV: activity in all organs and tissues simultaneusly.

- Possibility of acquiring images furing longer time (reveral radiotracer half lives)

  → Kinetic studies and dynamic images.

- Umprecedented quality.

Very high cost

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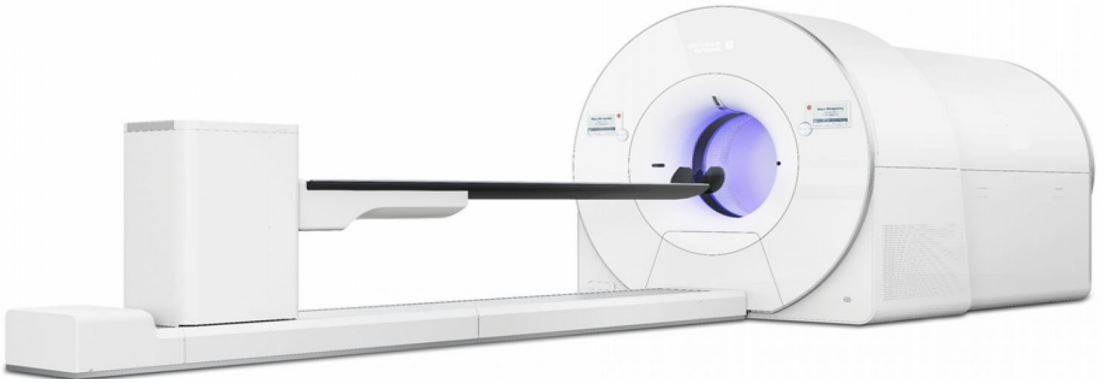
Total Body PET



EXPLORER
Whole body length

Biograph Vision Quadra
1 m length

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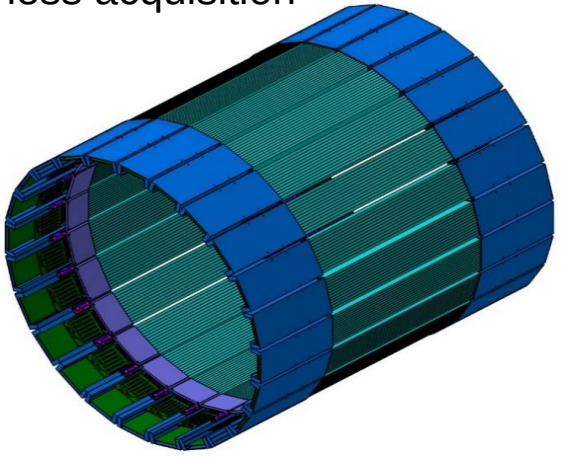
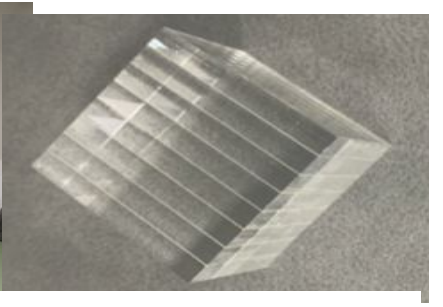
GVA NEXT

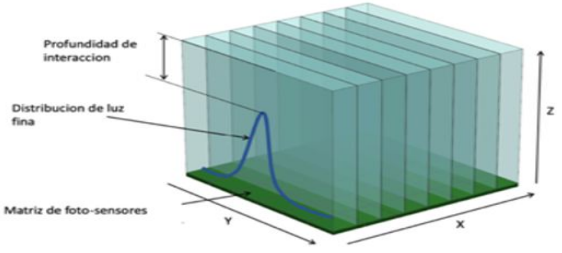
Total Body PET – affordable approaches

JPET: plastic scintillators
+ trigerless acquisition



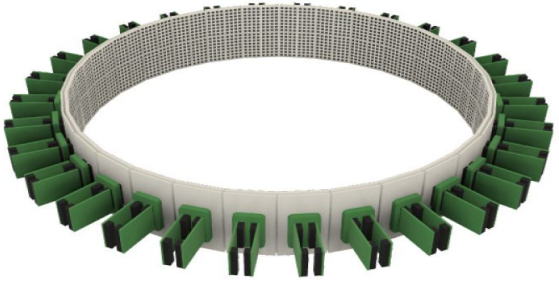
IMAS: semi-monolithic LYSO detectors

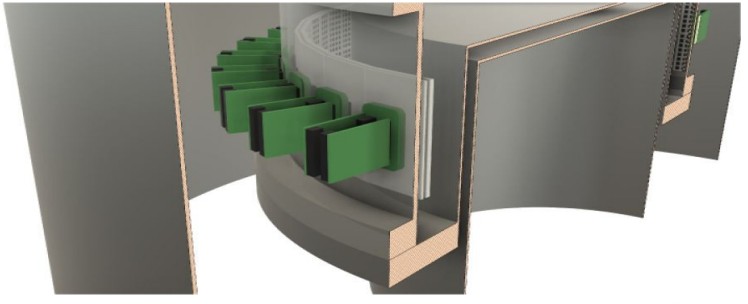




Courtesy of A. González

PETALO: liquid Xenon + SiPMs – continuous volume





Again BGO?
Other?

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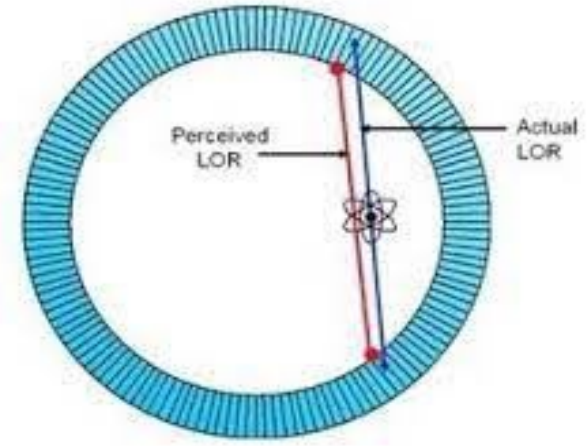
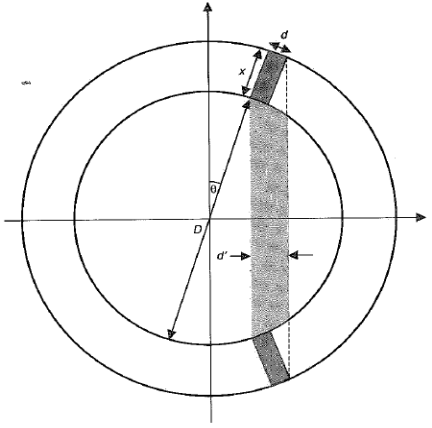
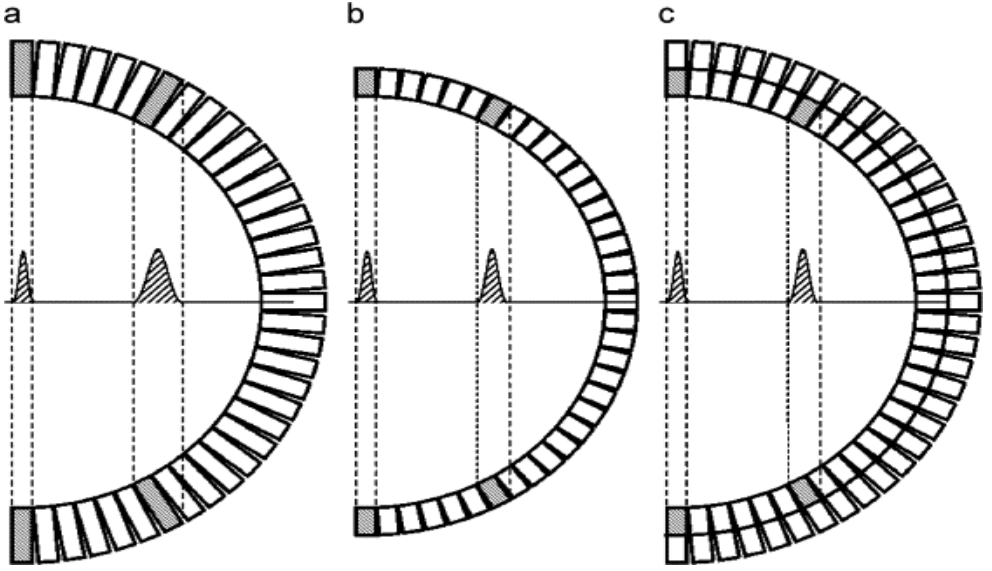
Depth-of-Interaction (DOI) determination





Parallax error degrades the resolution at the edges of the scanner



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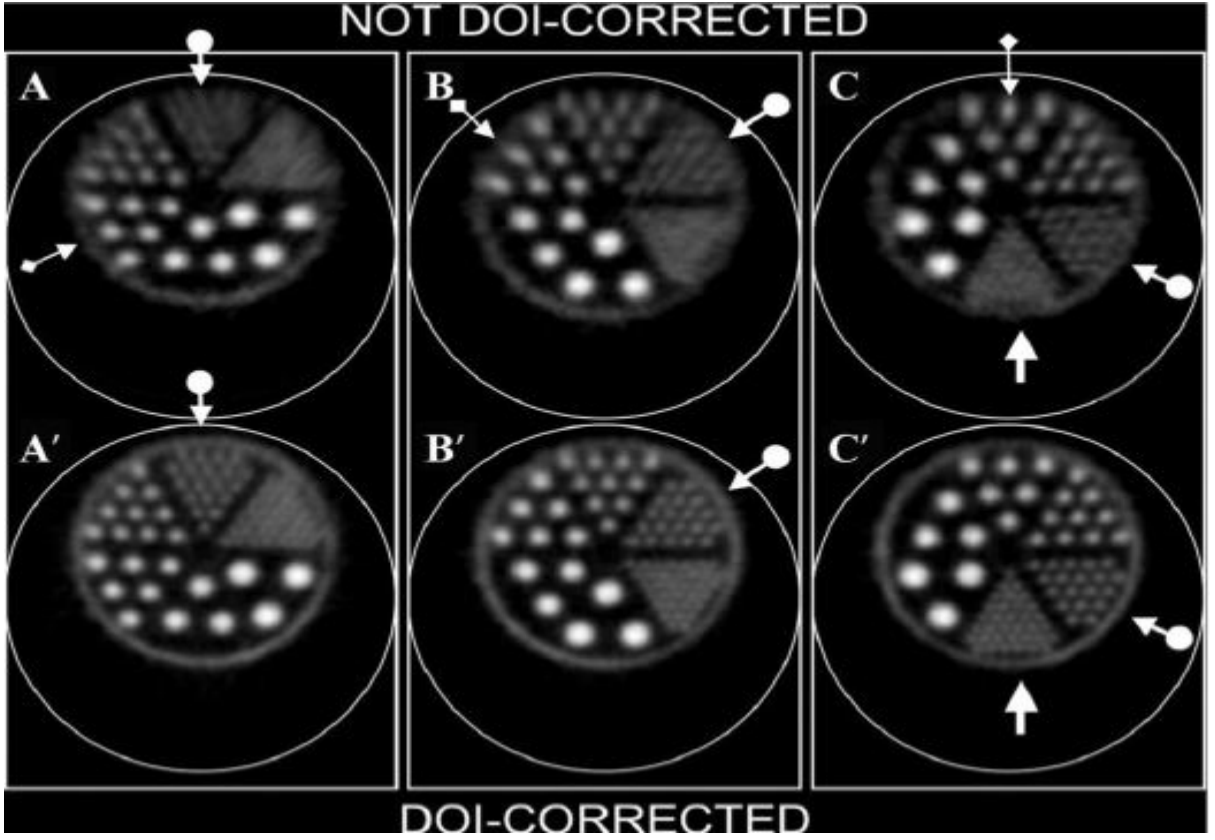
DOI determination



Green et al. Molec. Im. 9(6) 2010

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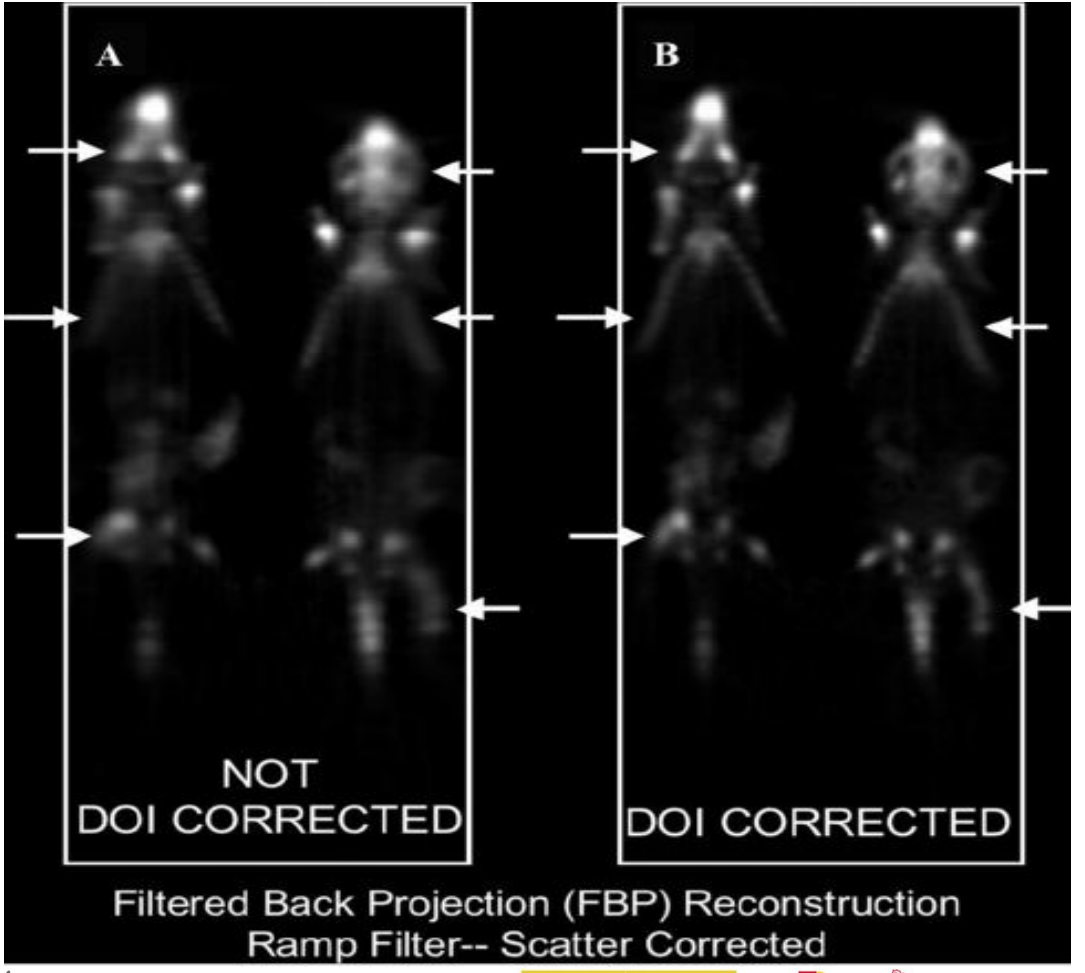
DOI determination



Green et al. Molec. Im. 9(6) 2010

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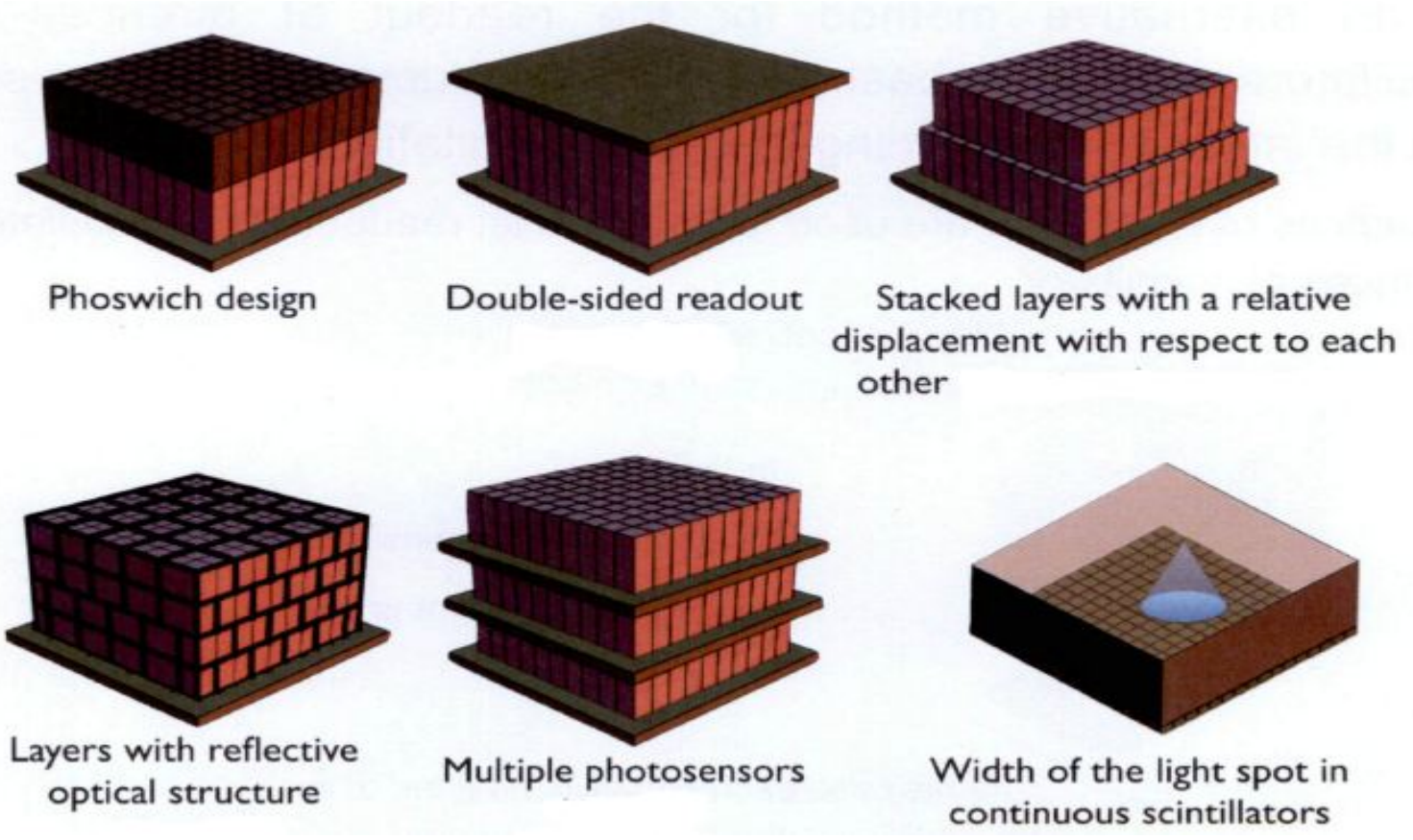
DOI determination



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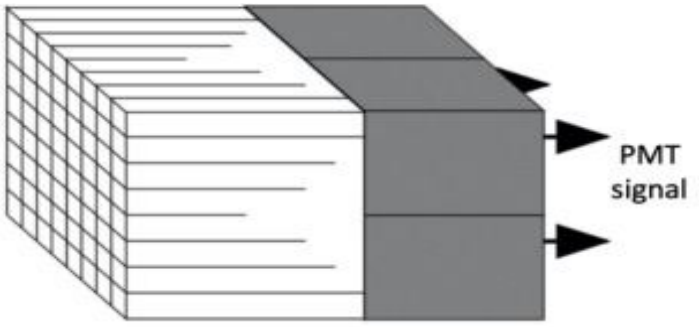
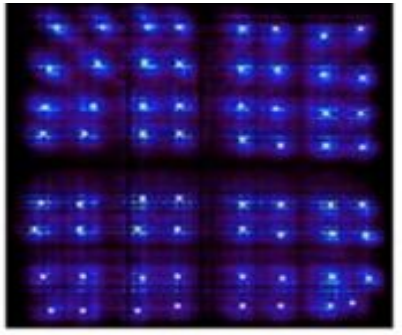
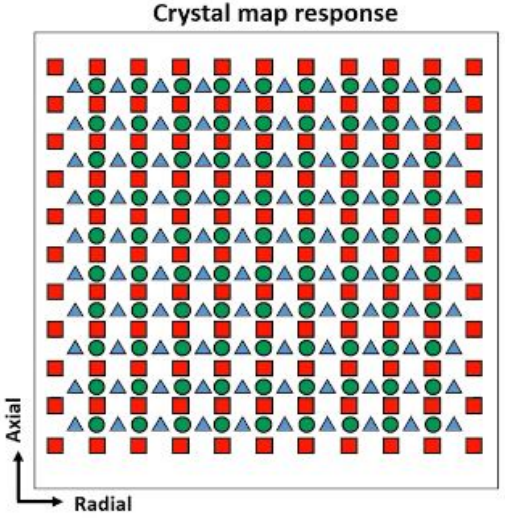
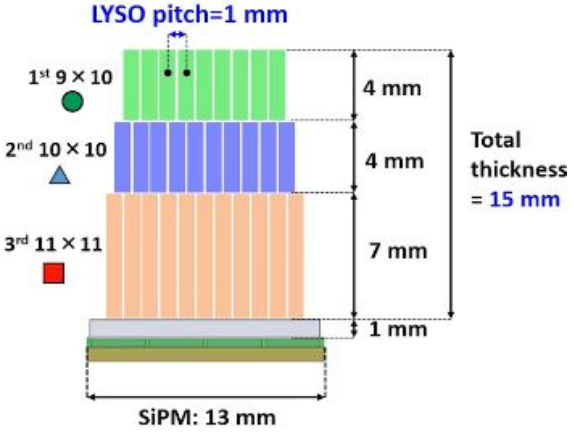
DOI determination









Higher cost
Generally not included in scanners

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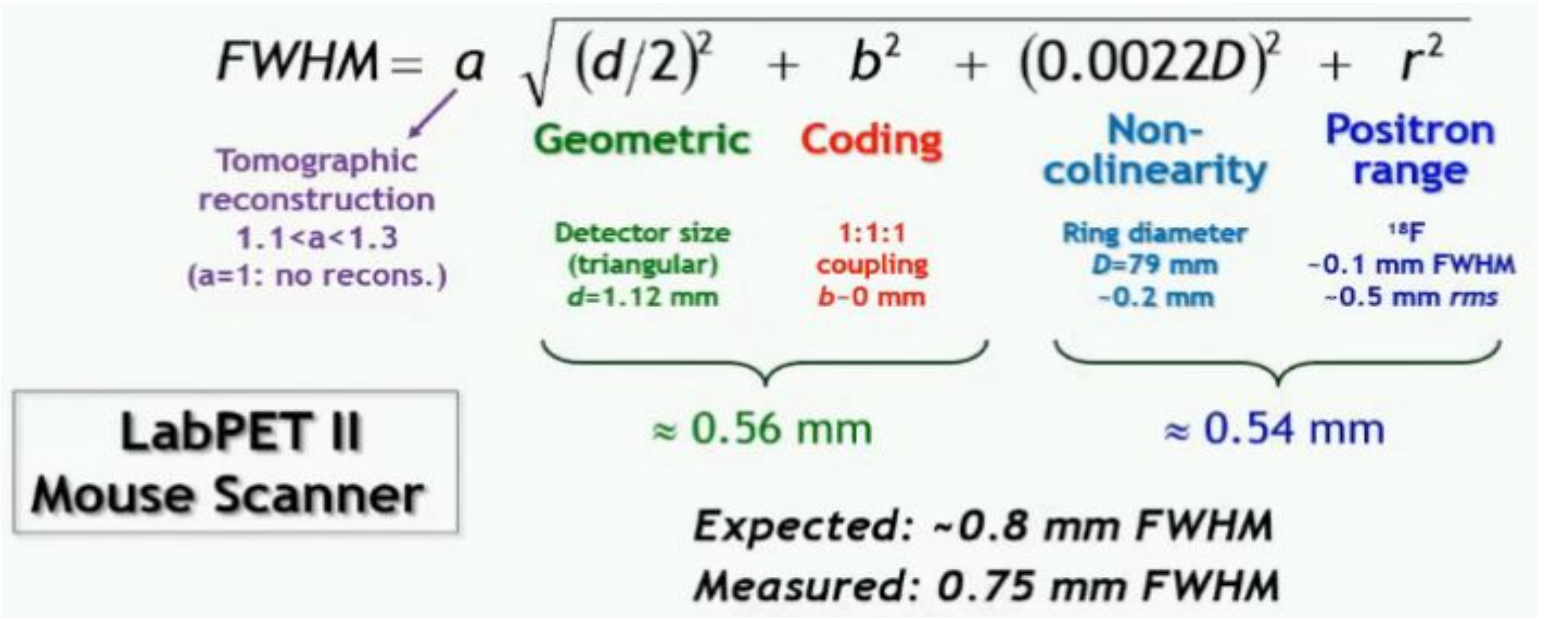
Spatial resolution



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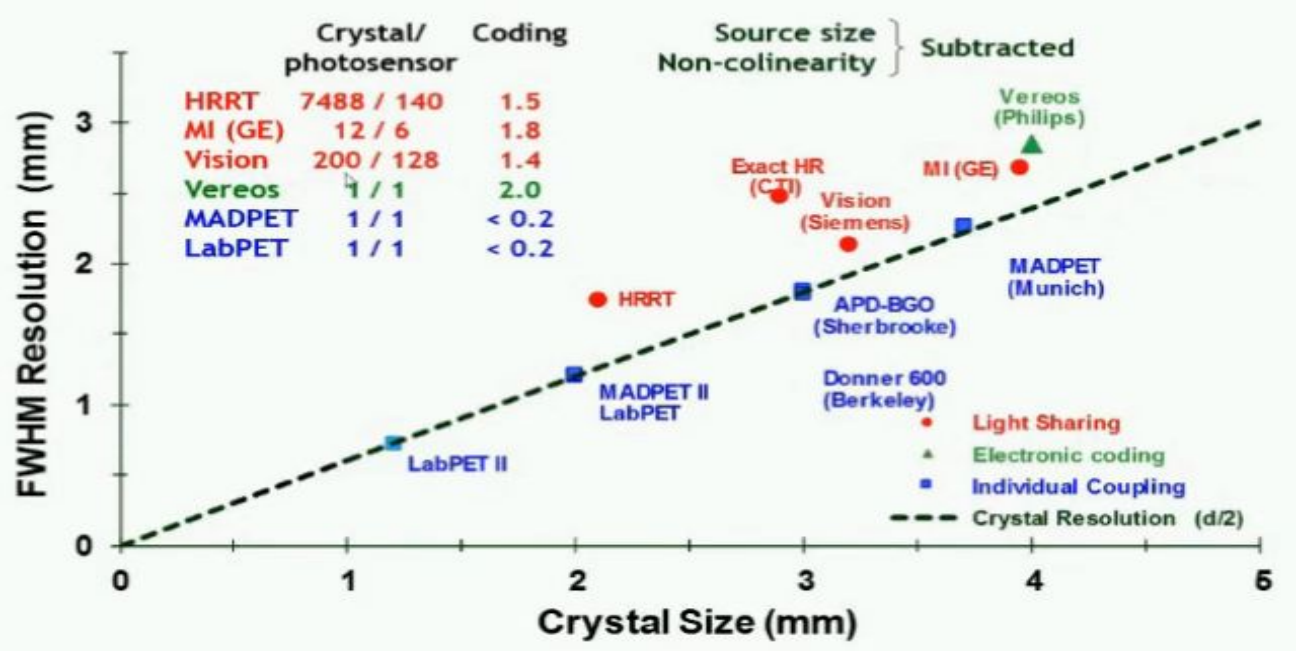
Spatial resolution in PET scanners

Small animal and dedicated scanners



- In clinical systems: 3-4 mm FWHM
- High resolution would allow to visualize tumour heterogeneity

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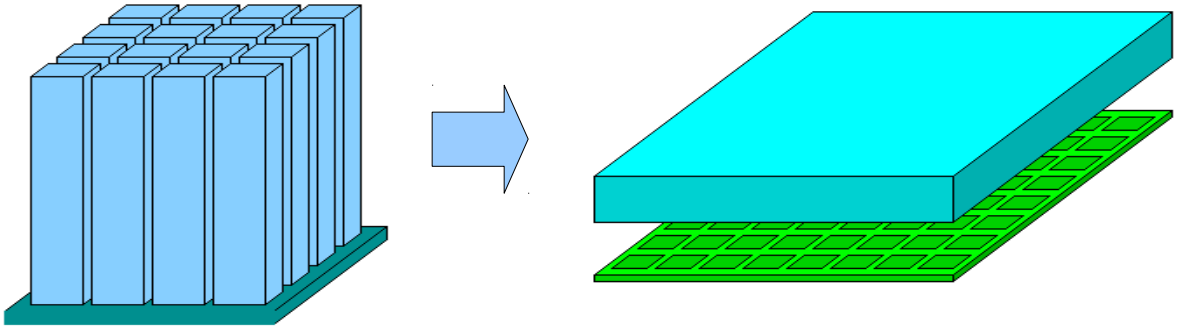
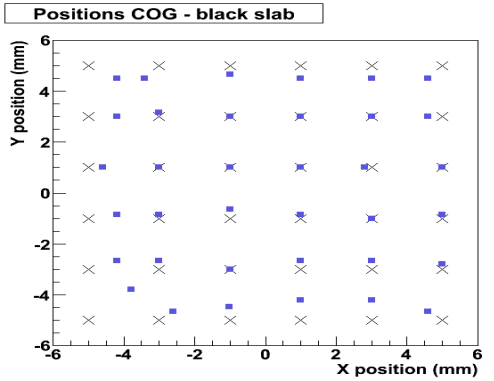
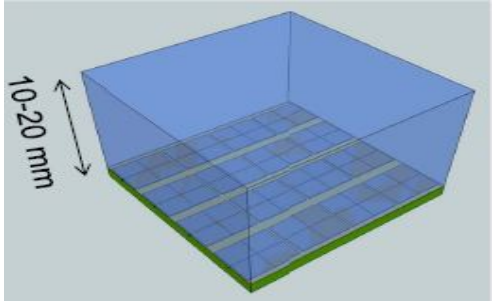
Monolithic detectors?







D. Schaart.
ICTR-PHE 2014

Neural Networks trained with Monte -Carlo simulations are promising

Performance parameter		Monolithic	State of the art
Energy resolution	(% FWHM)	11 - 12	~12
Spatial resolution	(mm FWHM)	1.0 - 1.6	4 - 6
DOI resolution	(mm FWHM)	3 - 5 mm	None
CRT	(ps FWHM)	160 - 185	500 - 650

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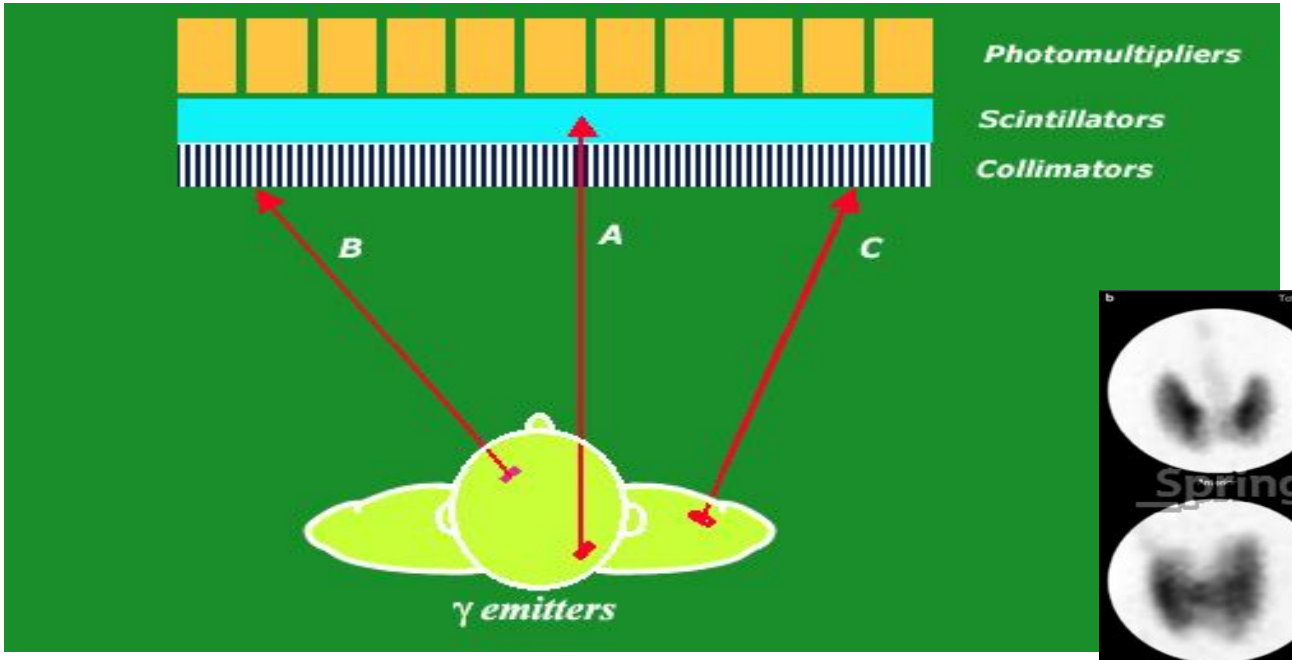
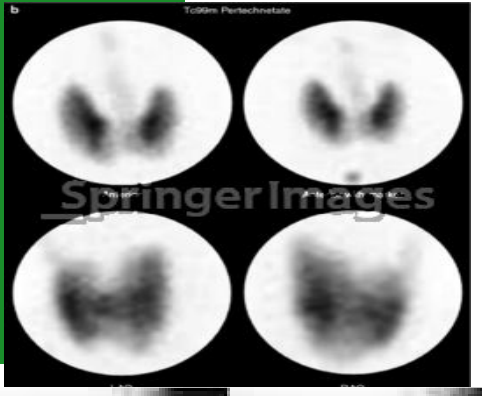
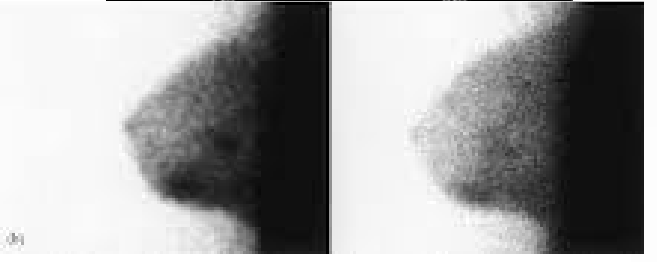
Gamma cameras







- Single photon emitters
- Most common radiotracer: ^{99m}Tc- 140 keV

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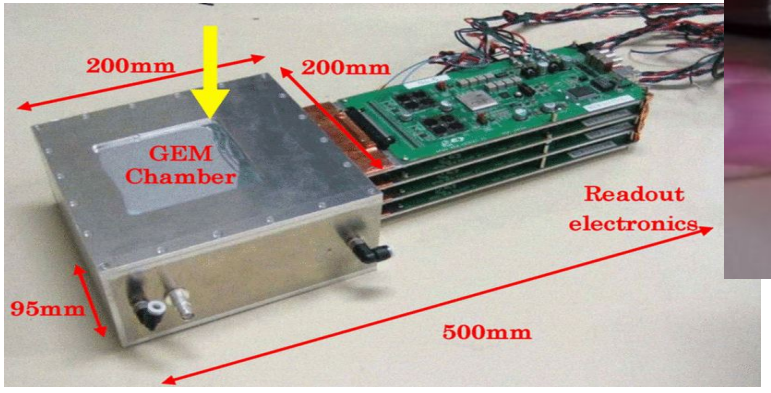
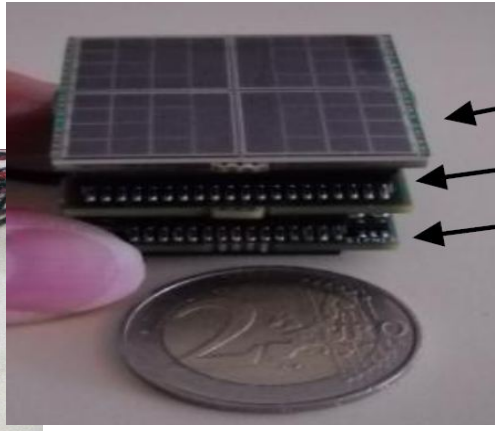
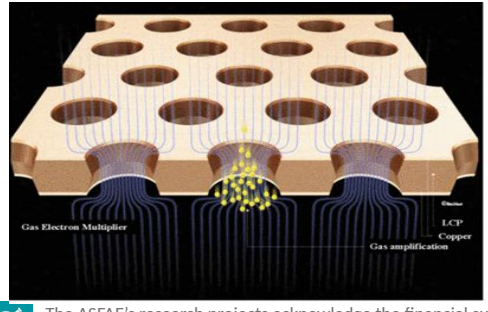
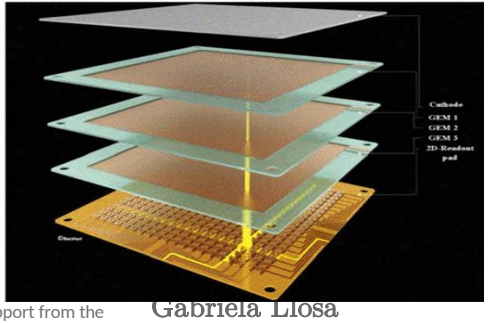
Gamma cameras

Small, dedicated systems (heart, breast…): mostly scintillators, but other types considered.









CZT, I. Blevis et al. 2011 IEEE NSS MIC conf record.
LaBr3, R. Pani et al 2015 JINST 10 C06002.
GEM- T. Koike et al. 2011 IEEE NSS MIC conf record.

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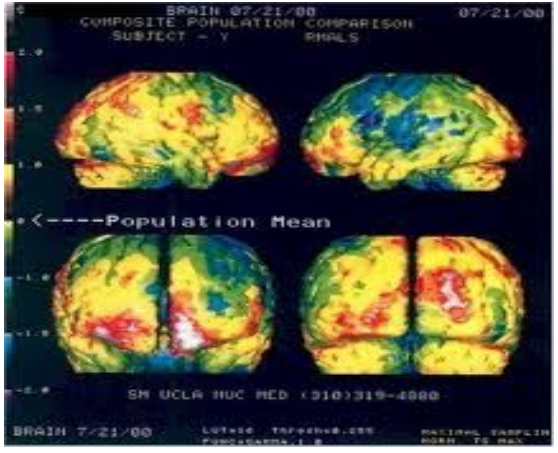
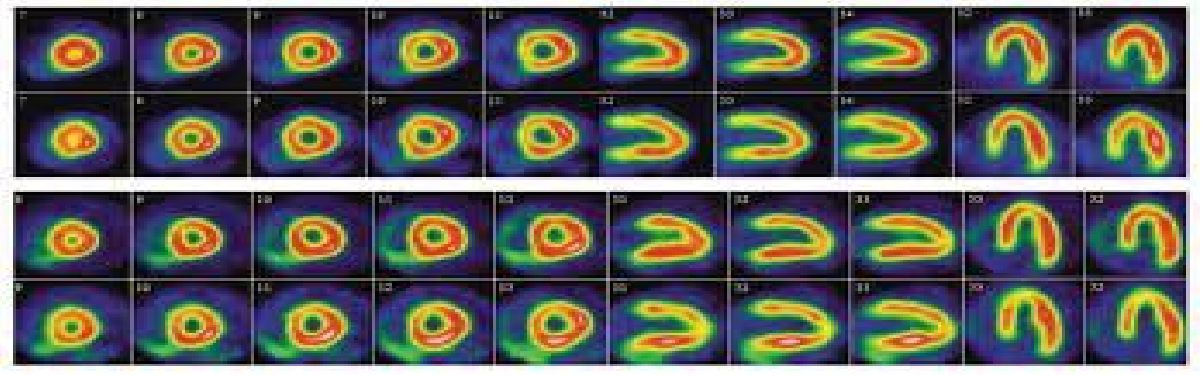
Single Photon Emission Computed Tomography (SPECT)

NM/CT 860 | GE HealthCare





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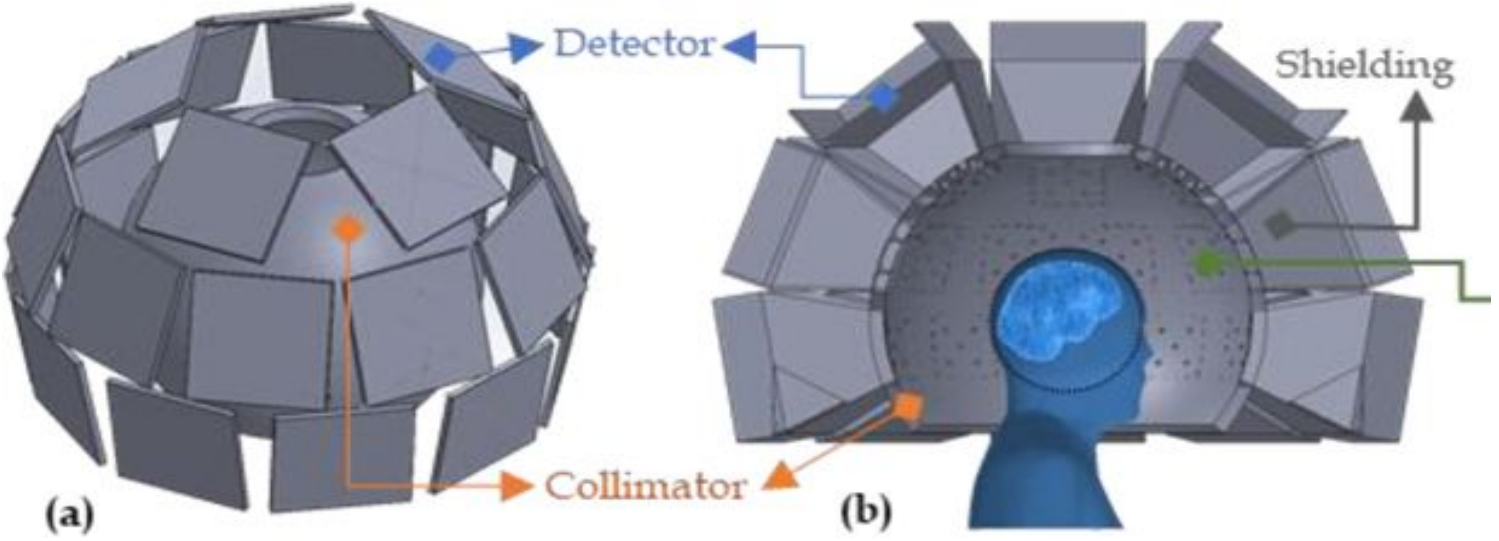
Dedicated systems

Mutipinhole brain SPECT



N. Zeraatkar et al. Biomed Phys Eng Express. 2021

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SPECT

Veriton-CT (Spectrum Dynamics Medical)

CZT detectors. Only SPECT, no gamma camera.

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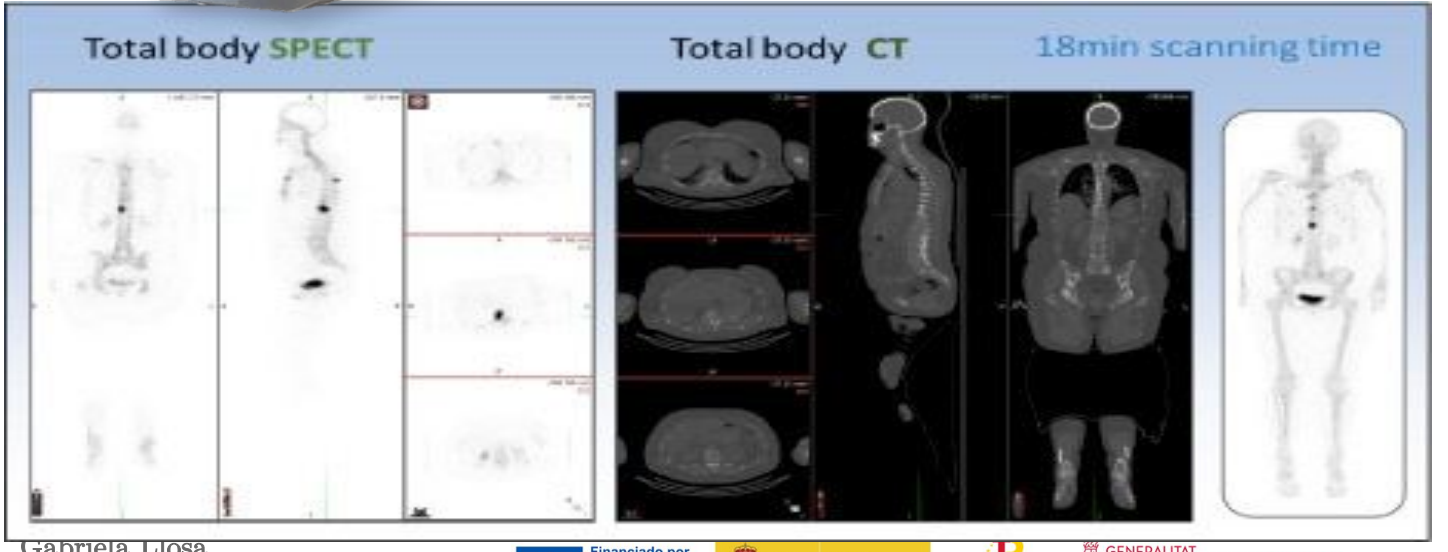
SPECT

Veriton-CT (Spectrum Dynamics Medical)



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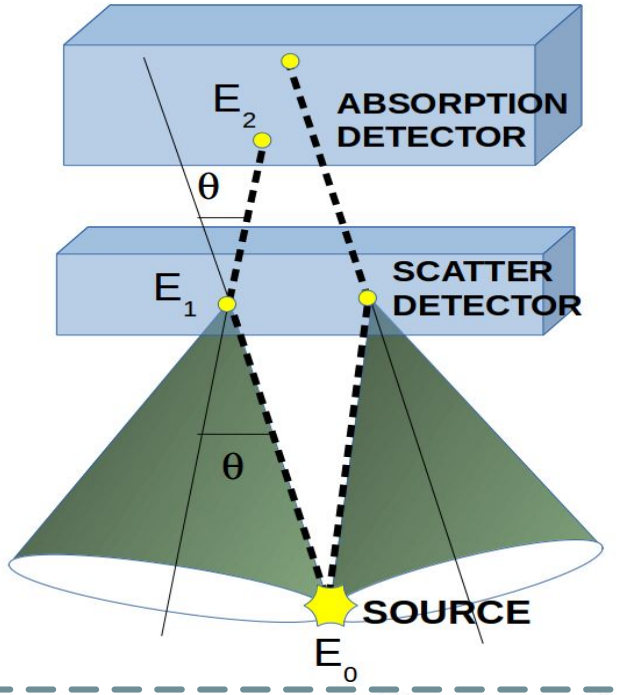
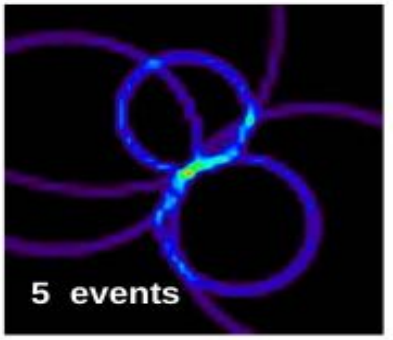
Compton cameras

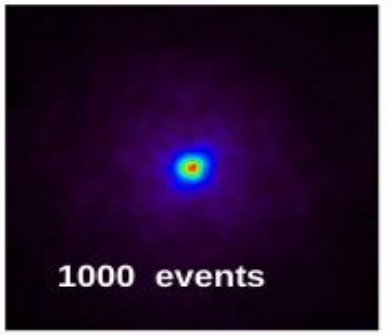


$$\cos\varphi = 1 - m_0c^2\left(\frac{1}{E_{\gamma'}} - \frac{1}{E_\gamma}\right)$$

$$E_\gamma = E_{e^-} + E_{\gamma'}$$

Backprojection





+ Image reconstruction

- Higher efficiency than gamma cameras
- Better at higher energies
- Better for multiple energies

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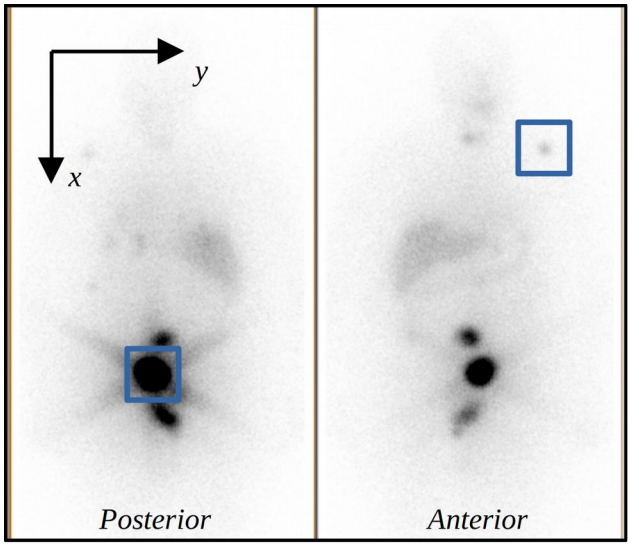
Compton cameras for radionuclide therapy assessment

- Radionuclide therapy is expanding due to its good results.
- Imaging can be used to visualize their distribution in the body and carry out dosimetry employing secondary gamma radiation.
- More challenging than diagnostic imaging since photon energies and activities are not optimized for gamma cameras.
- Particularly complicated for alpha emitting radionuclides due to low activities and high photon energies.
- Compton cameras, initially developed for astroparticle physics experiments, can overcome the difficulties encountered by gamma cameras.
  - Higher efficiency.
  - Better suited for high energy photons.
  - Better suited for multi-gamma emission.



Gamma camera images of a patient treated with ^{131}I-NaI.

Compton cameras are a promising tool for theranostics

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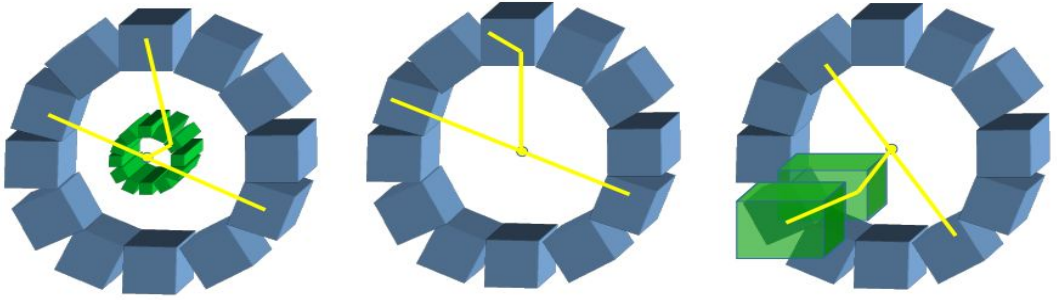
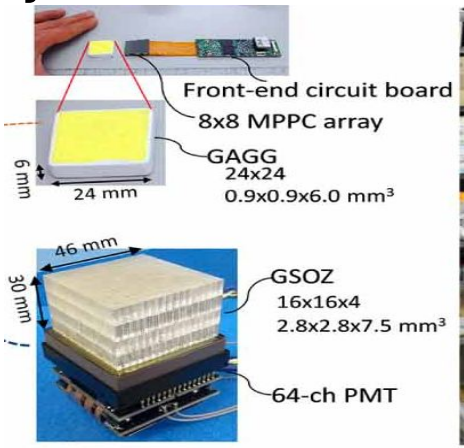
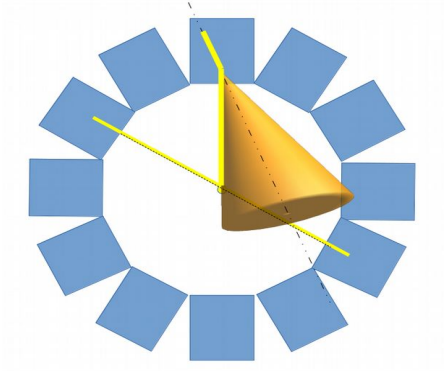
Compton-PET / WGI

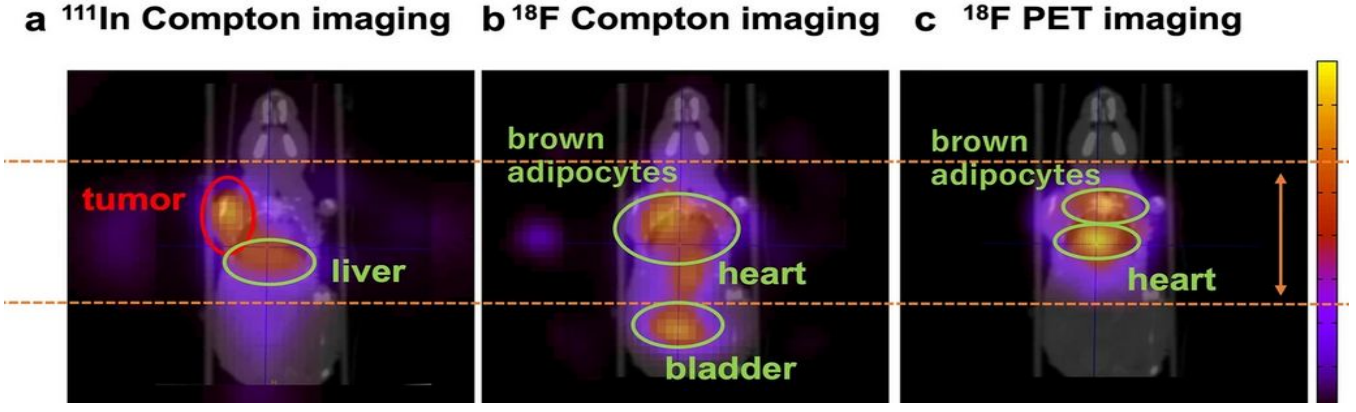
PET and gamma tracers simultaneously







Three gamma imaging ^{89}Zn



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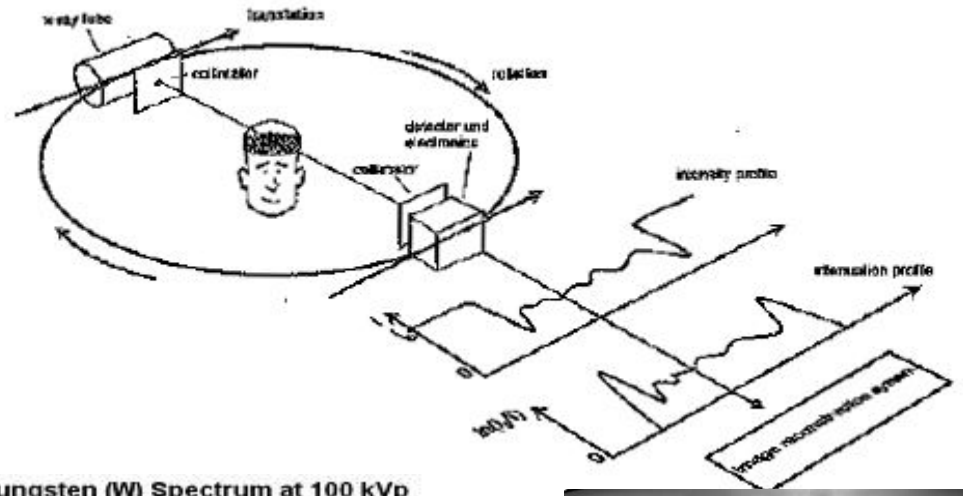
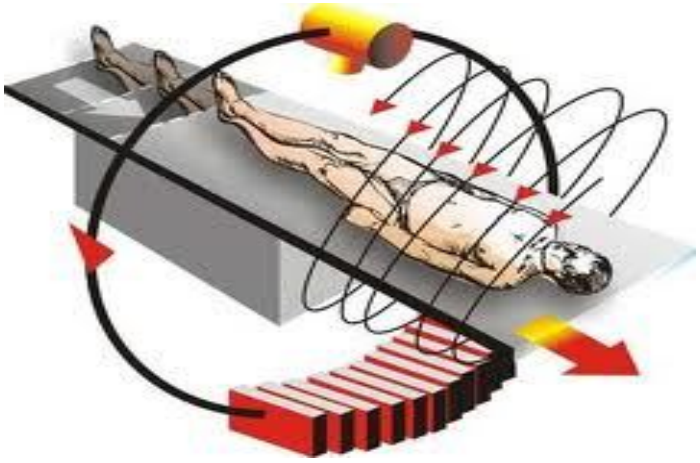
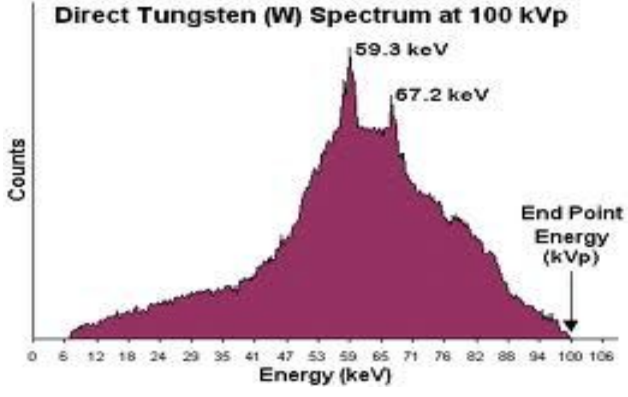
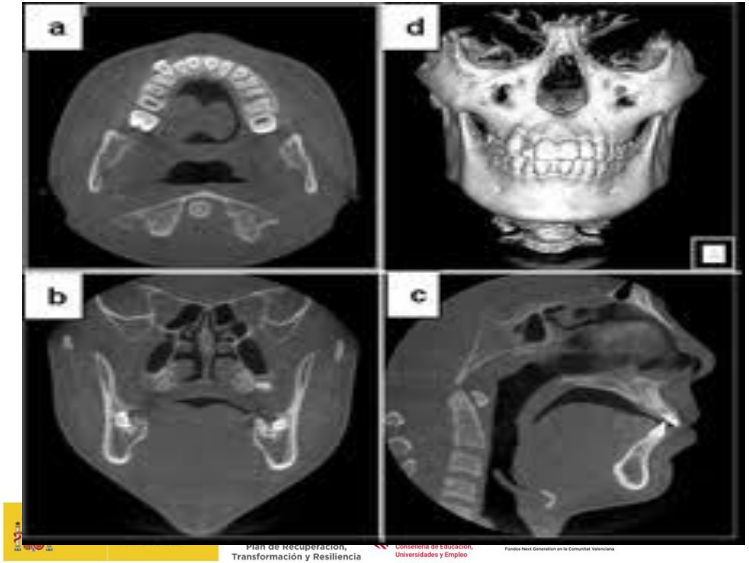
X-rays and Computed Tomography (CT)









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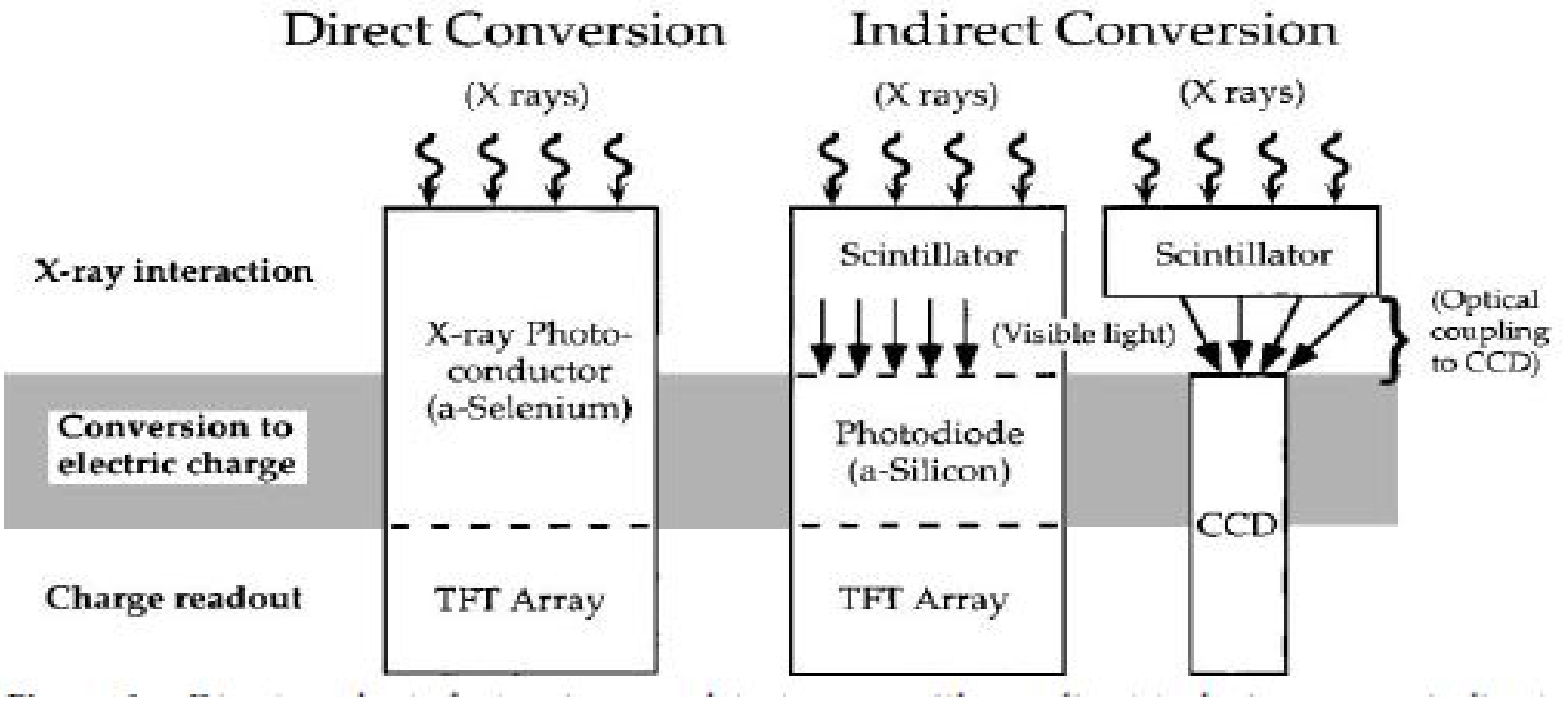
CT detectors



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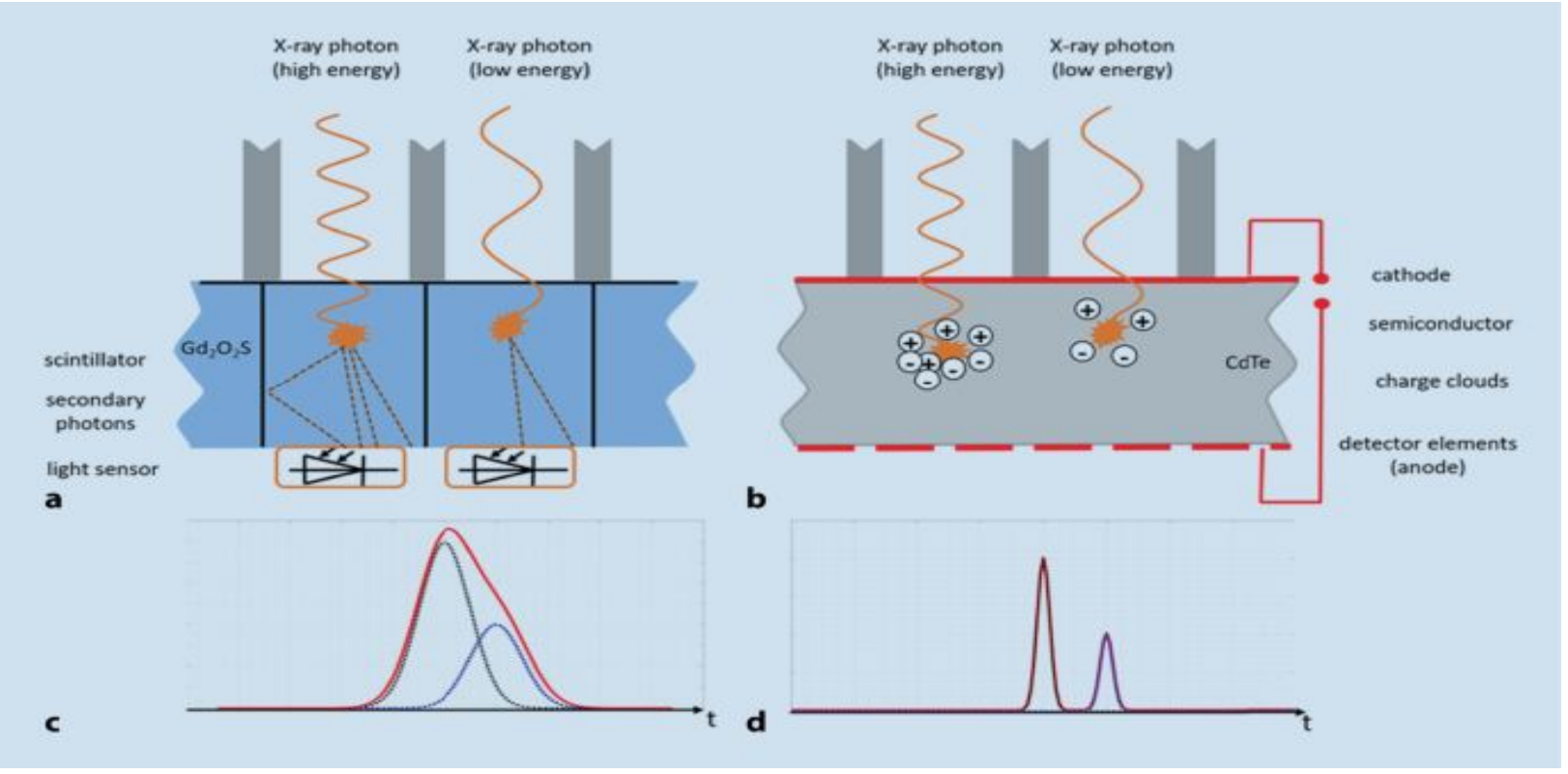
Photon counting CT



Quantify the energy of each individual photon

→ Images at different energies and reduced noise

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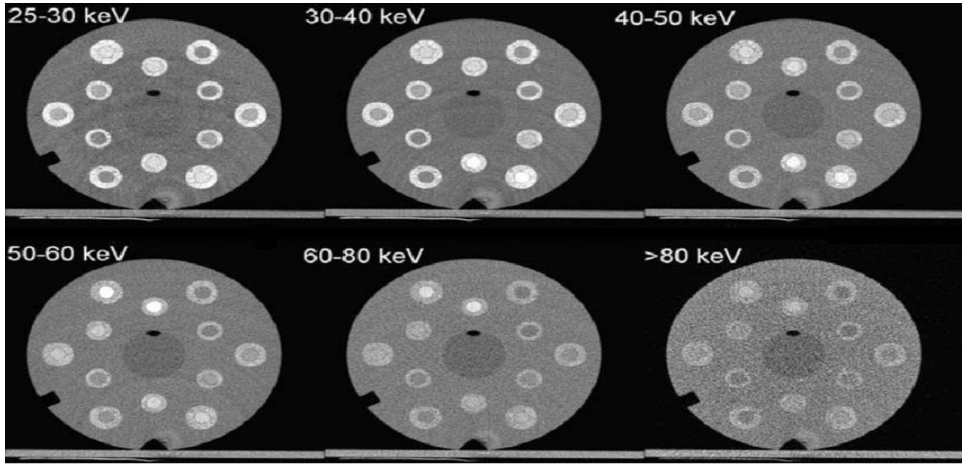
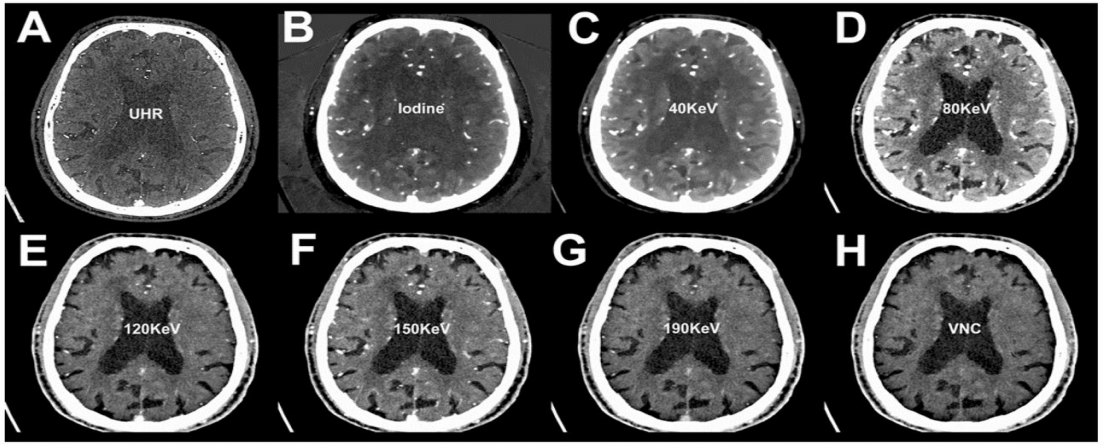
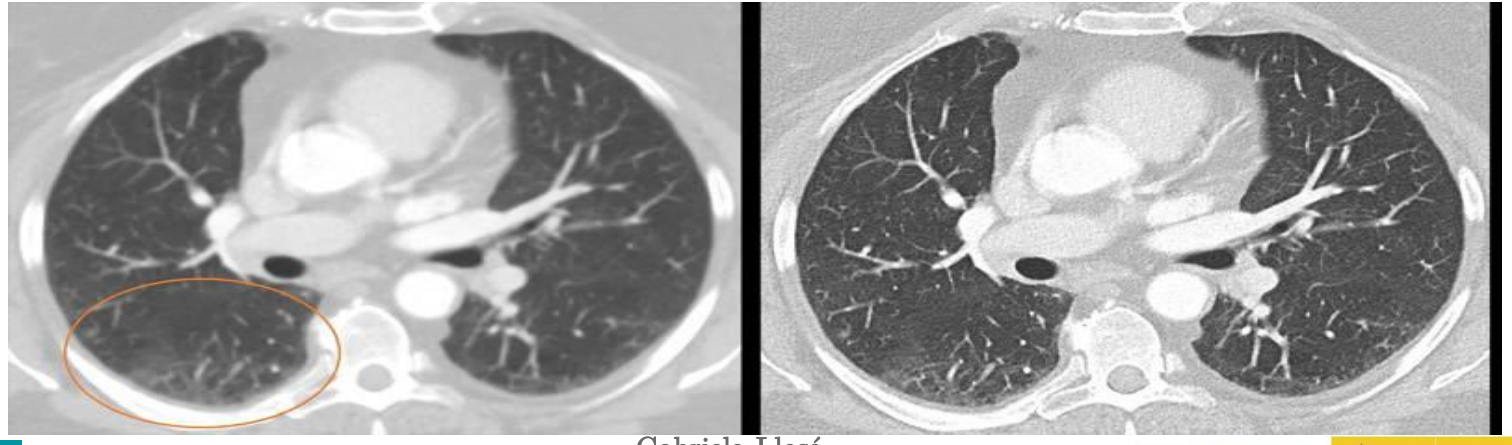
Photon counting CT





Conventional CT

Photon counting CT



Possible with scintillators? $LaBr_3$?

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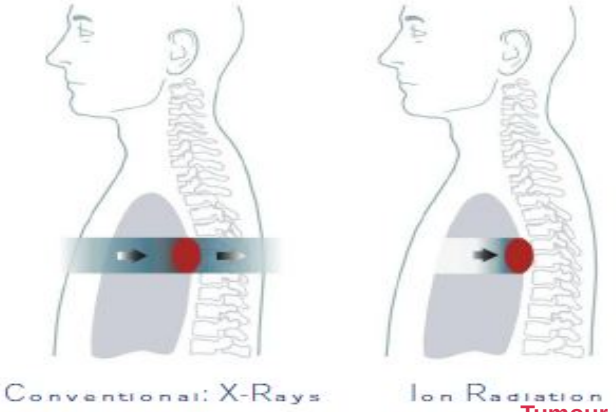
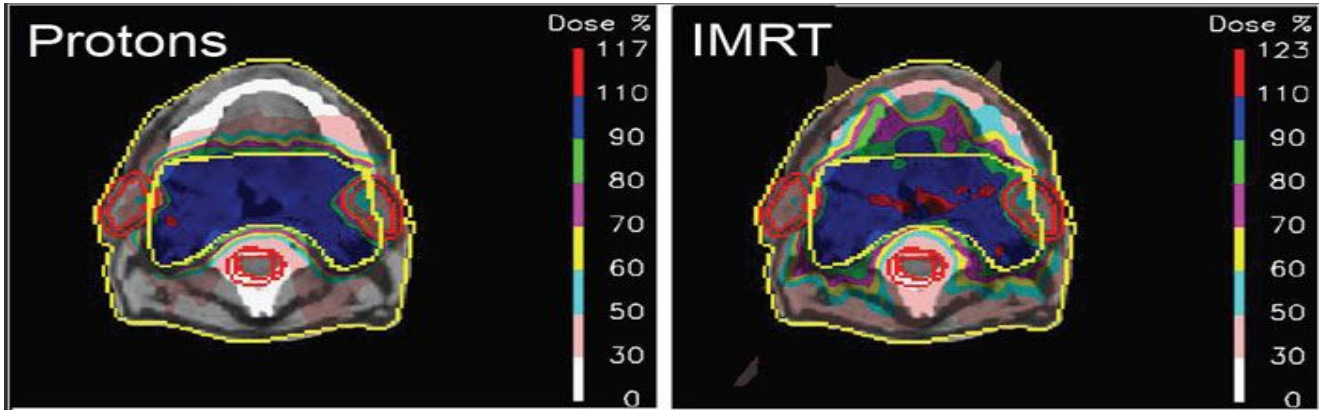
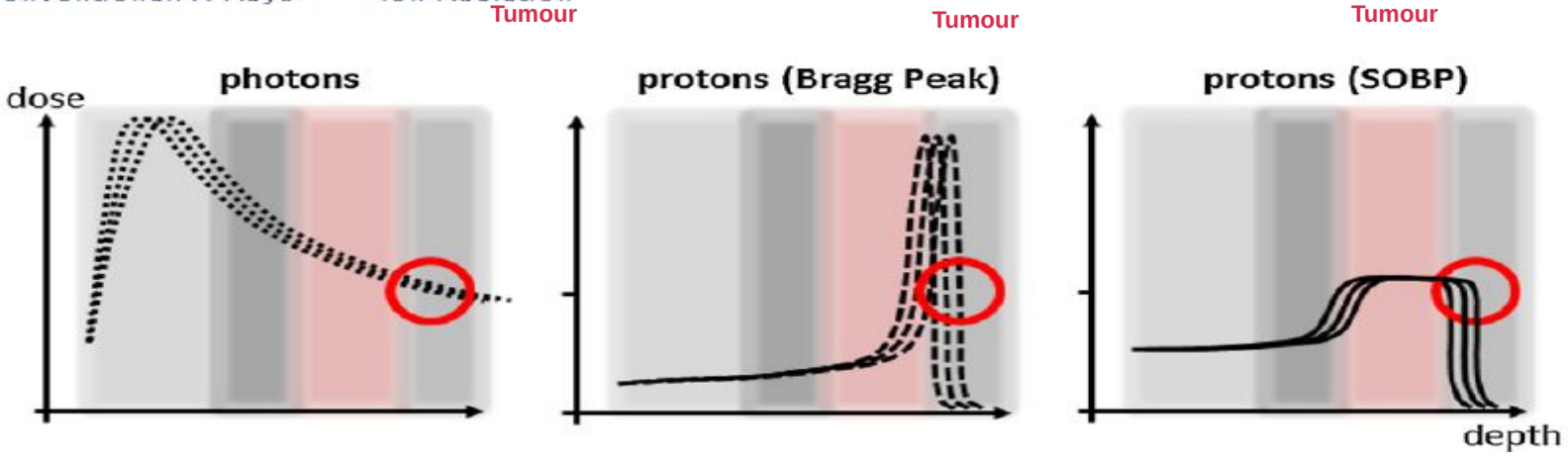
Hadron therapy treatment monitoring







Large safety margins applied to treatment plans.

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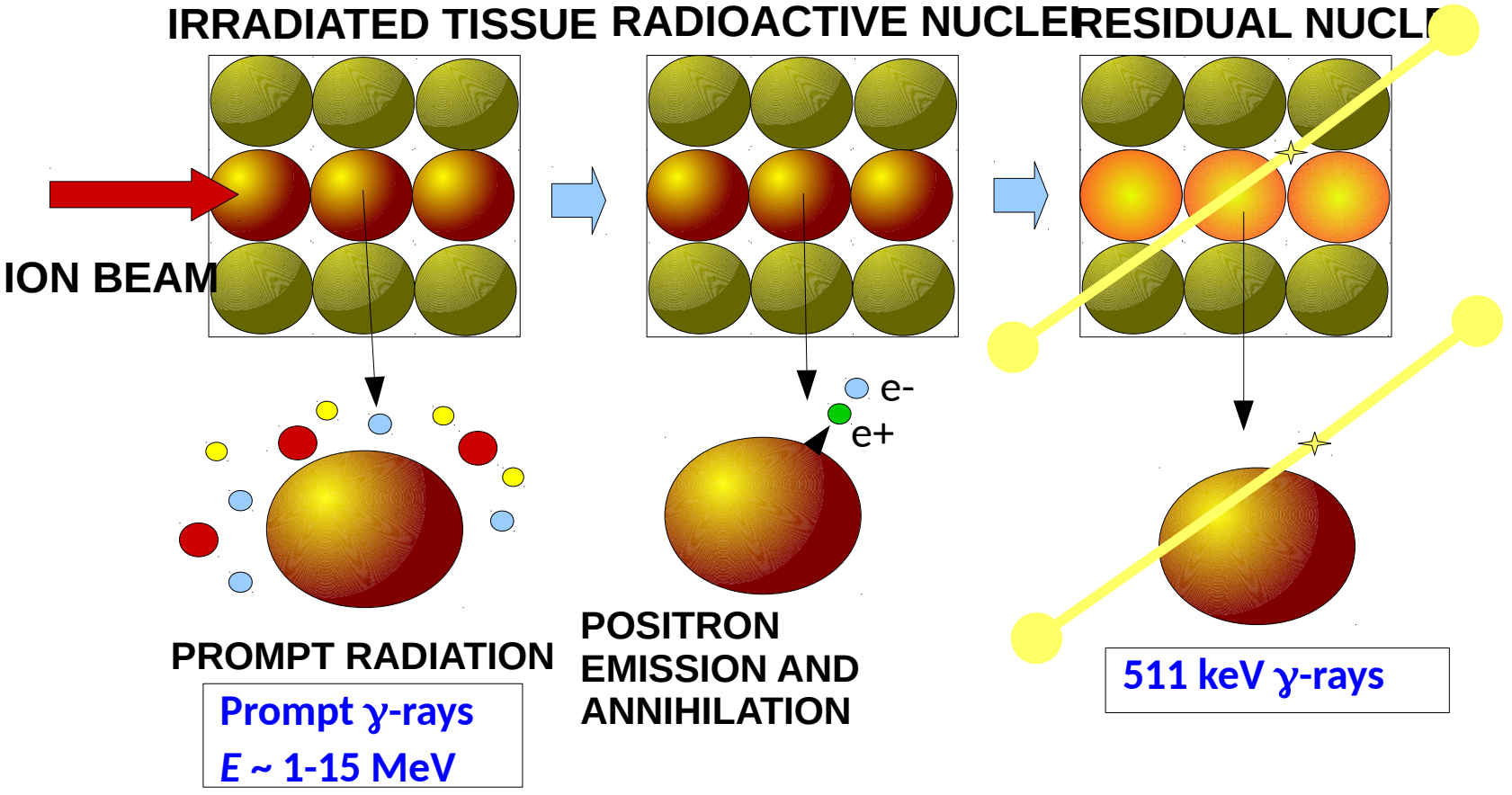
Hadron therapy treatment monitoring



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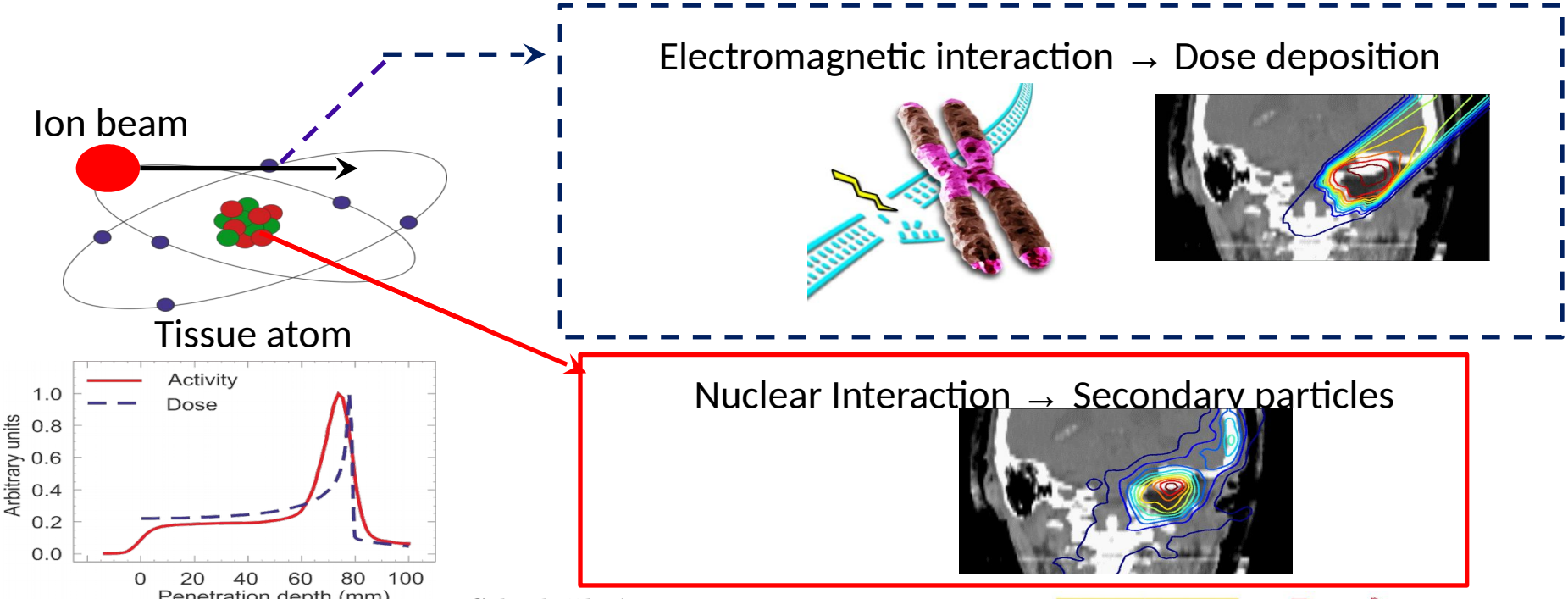
Treatment monitoring

- Dose deposition through electromagnetic interaction.
- Monitoring through secondary particles emission (nuclear interactions).
- Different, but correlated quantities. Indirect measurement.



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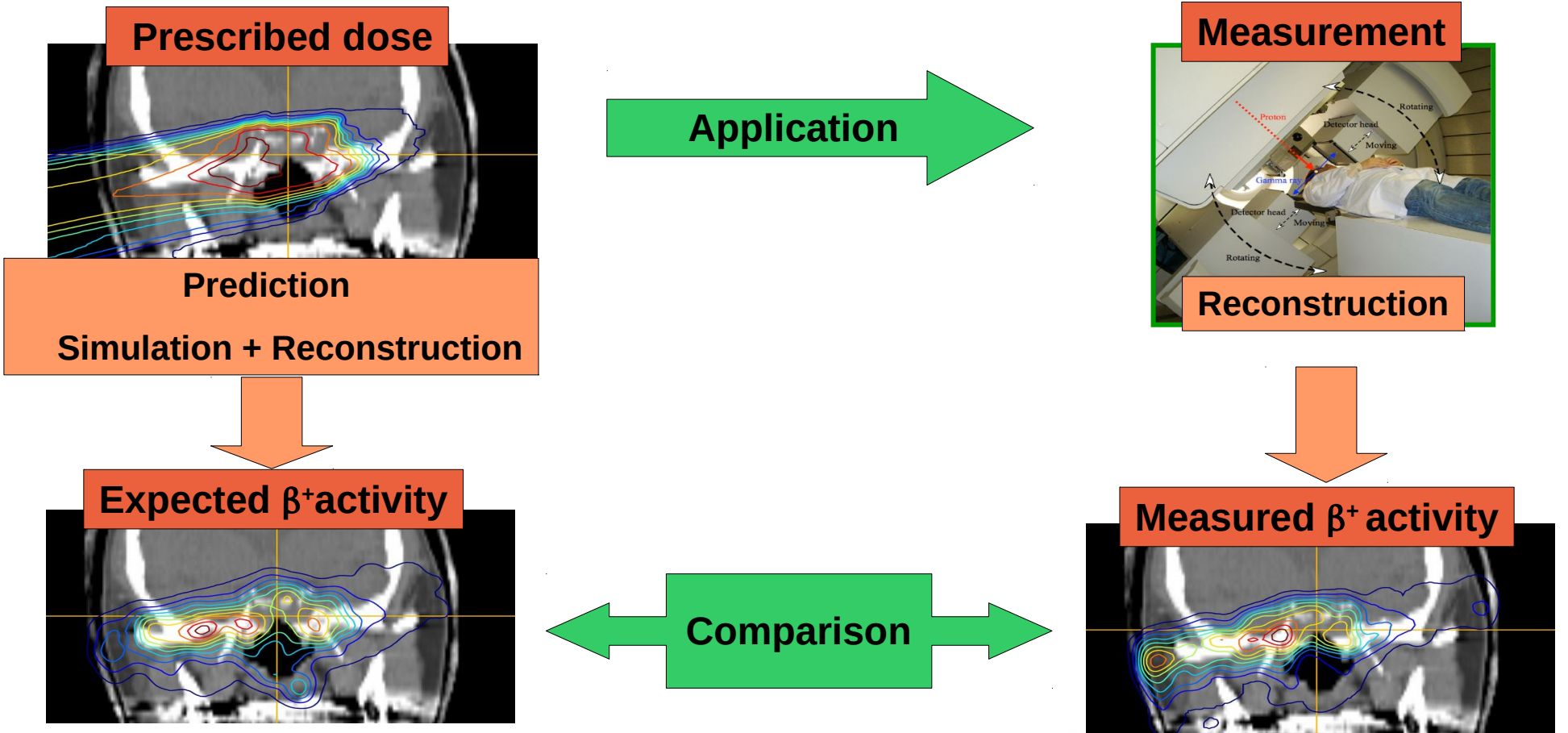
Monitoring with PET



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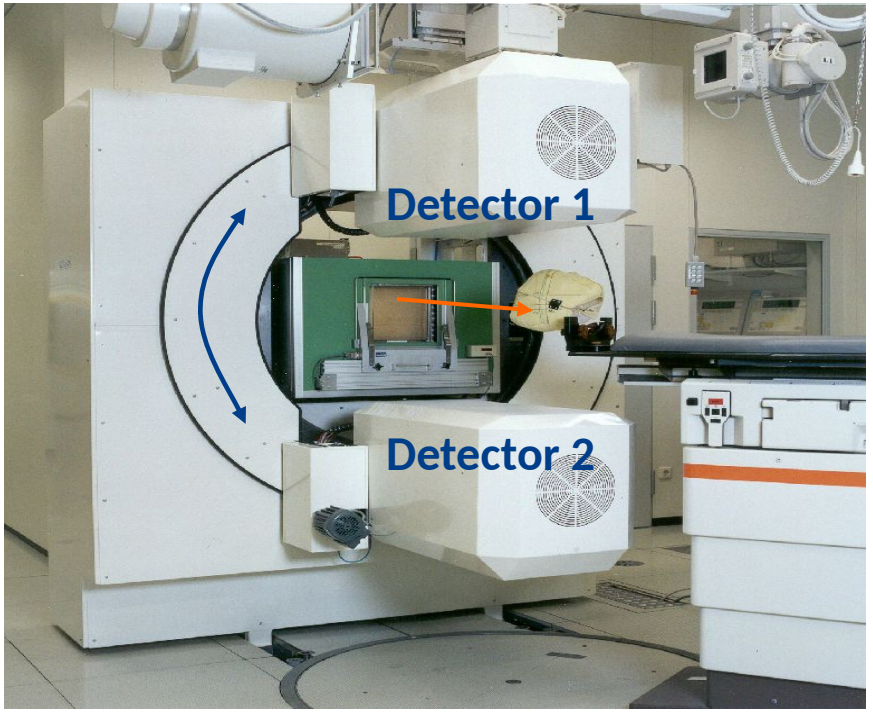
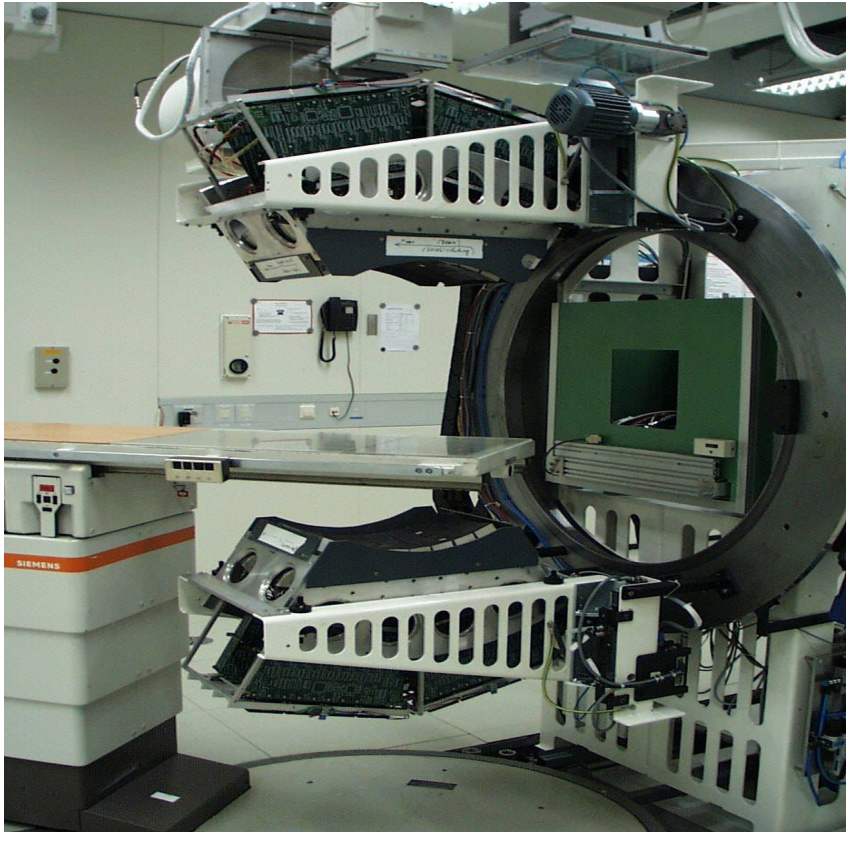
Monitoring with PET



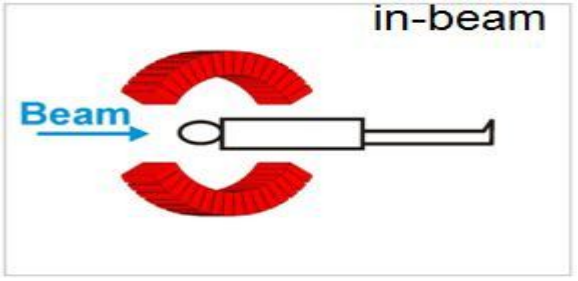


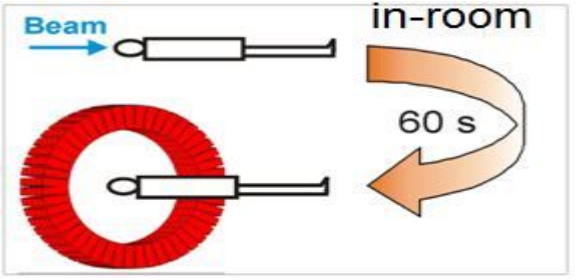
PT PET Scanner @ GSI

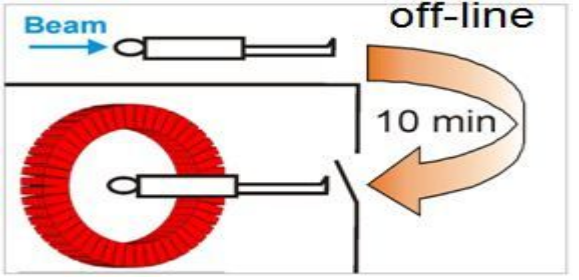
The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Modalities

→ Higher influence of the metabolism, lower beta activity →





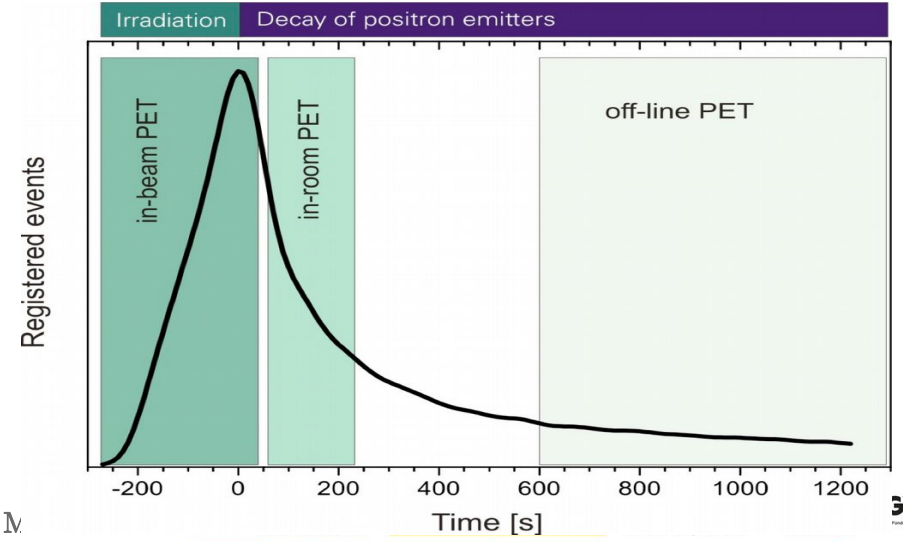


Measurement during irradiation

Measurement shortly after the irradiation

Measurement some time after irradiation

IN-BEAM	*OPEN*
IN-ROOM	*OPEN* *FULL*
OFF-LINE	*FULL*



The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

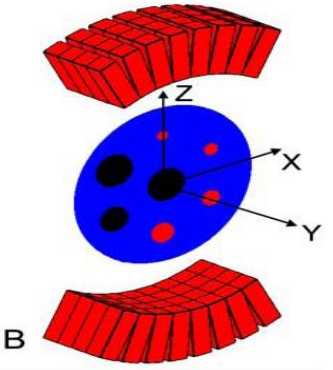
PET Limitations

- Positron production does not follow irradiation immediately.
- Biological washout- activity carried away by metabolic processes.
- Low amount of β+ activity induced- low efficiency.
- Difficult online studies – partial ring.
- Photons produce significant background.

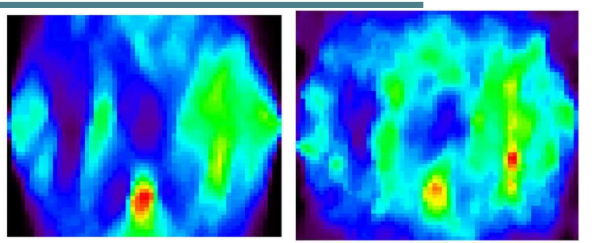
The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Research

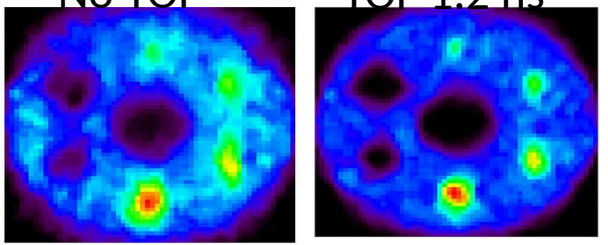
- Models for washout.
- Use of short-lived isotopes.
- TOF PET to minimize gap effects.
- PET integration with the gantry.



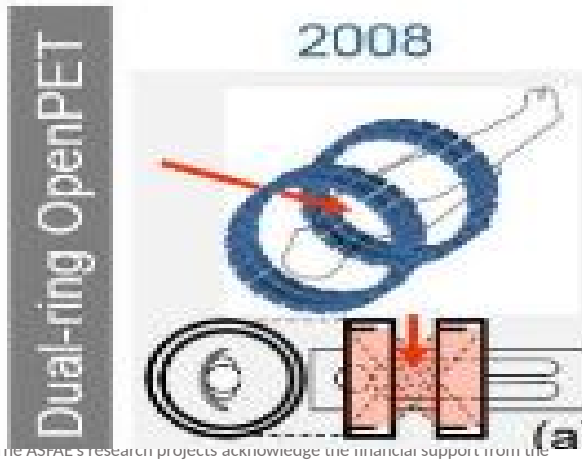
P. Crespo et al.,
Phys. Med. Biol. 51

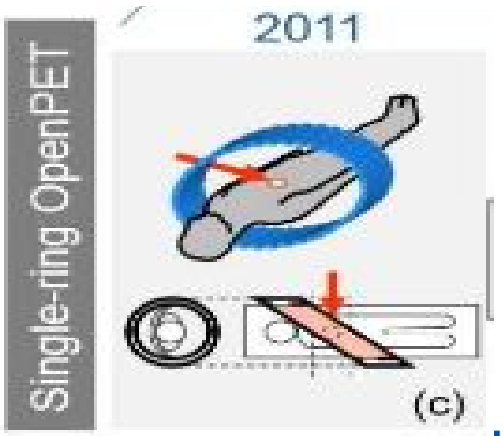


No TOF TOF 1.2 ns



TOF 1.2 ns TOF 0.1ns





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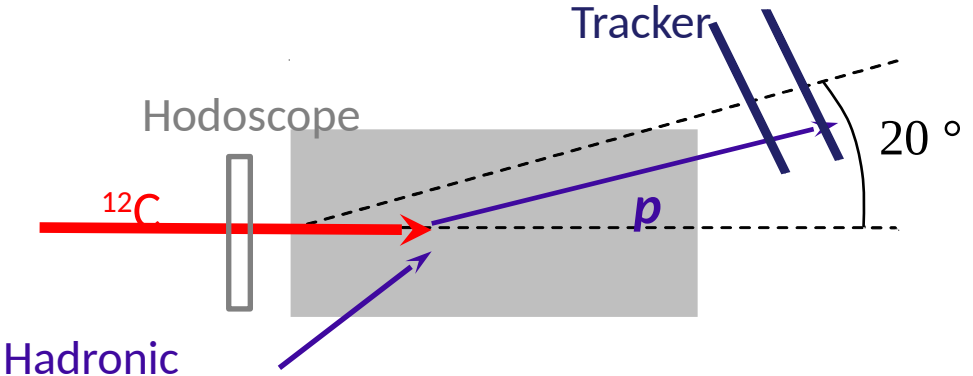
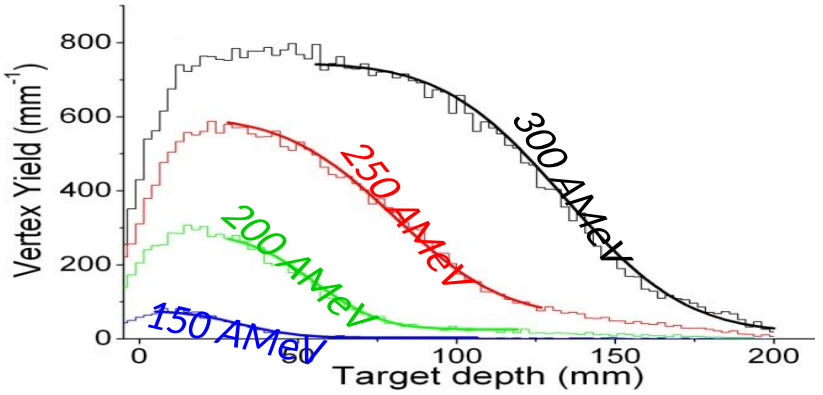
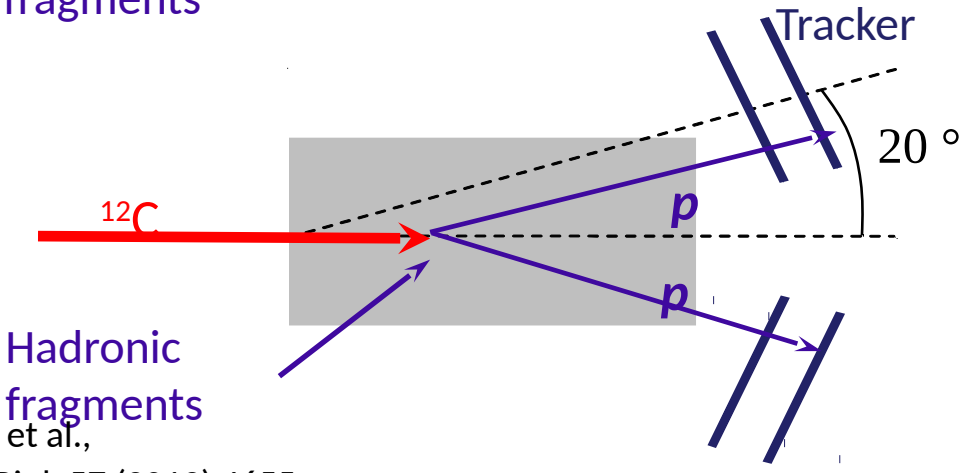
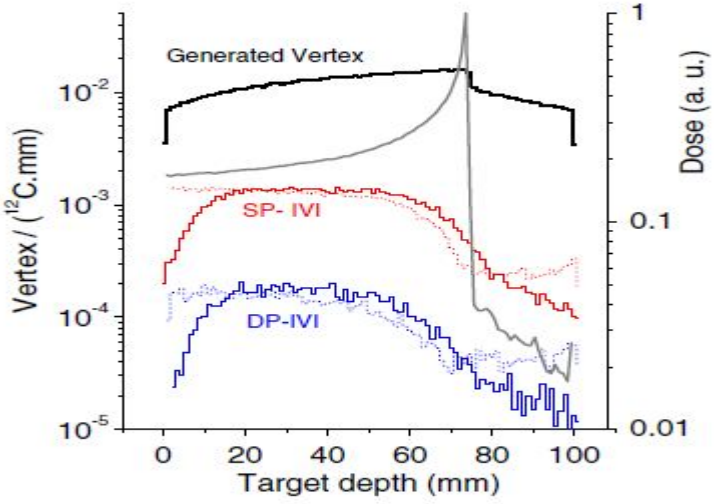
Monitoring with secondary charged particles

Interaction Vertex Imaging (mainly Carbon ions)







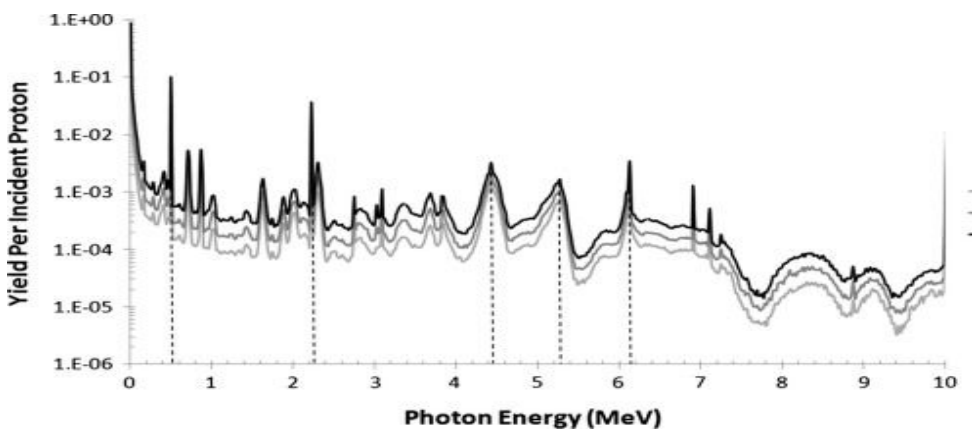


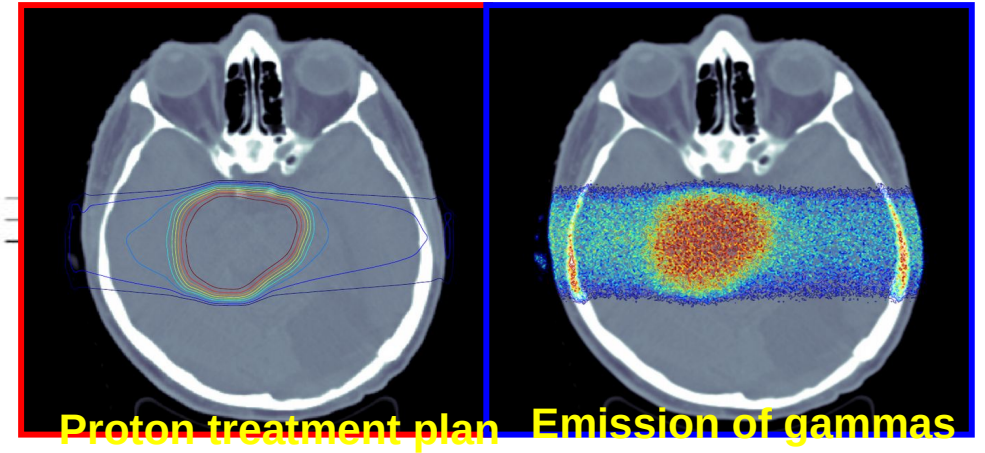
P Henriquet et al.,
Phys. Med. Biol. 57 (2012) 4655

This ASFAE's research project is acknowledging the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Monitoring with prompt gammas

- Most promising approach nowadays
- Emission ~ns after irradiation.
- ~ 7 x more photons /cGy than positrons.
- Emitted in a continuous energy spectrum in the MeV range with characteristic peaks.



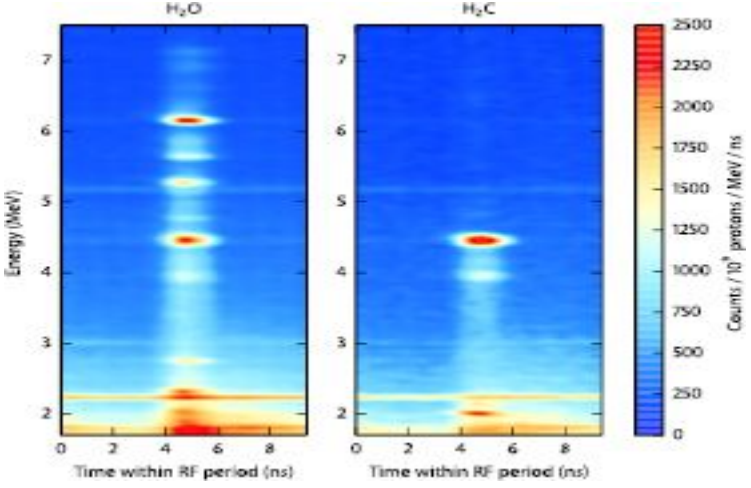


The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Prompt gamma spectroscopy

- Measure differential cross sections for 15 prompt gamma-ray lines from proton-nuclear interactions with ^{12}C and ^{16}O at proton energies up to 150 MeV.
- Model discrete prompt gamma-ray emissions along proton pencil-beams.
- Fit detected prompt gamma-ray counts to these models, simultaneously determine the beam range and the oxygen and carbon concentration of the irradiated matter.

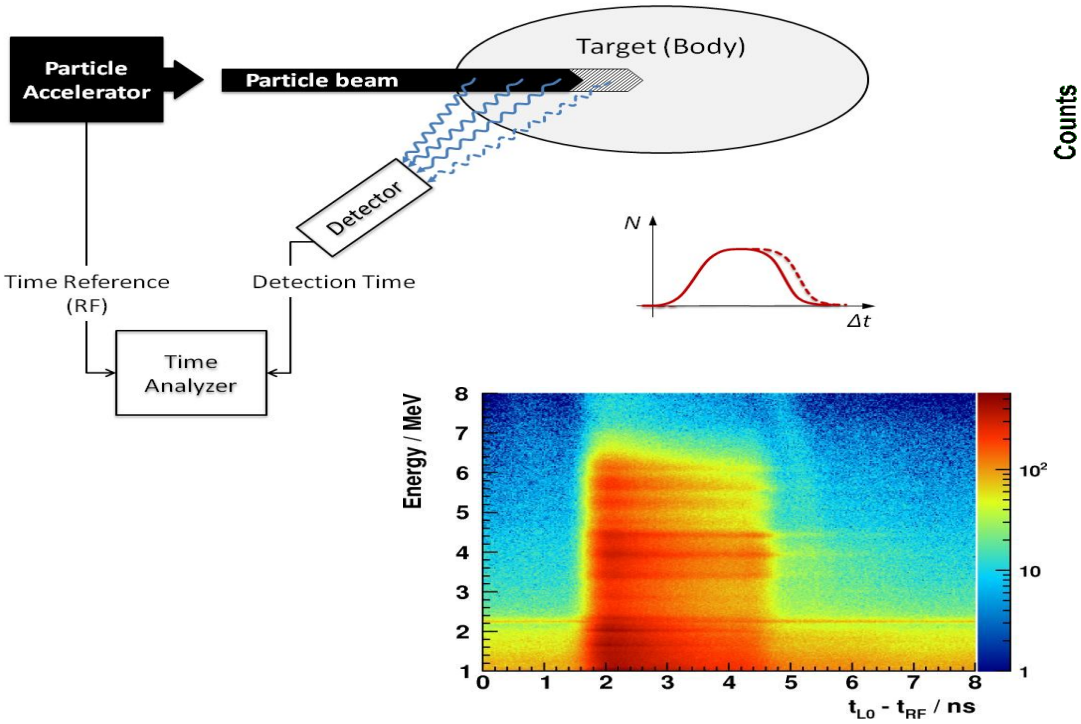
Verburg et al. PMB 58 (2013).

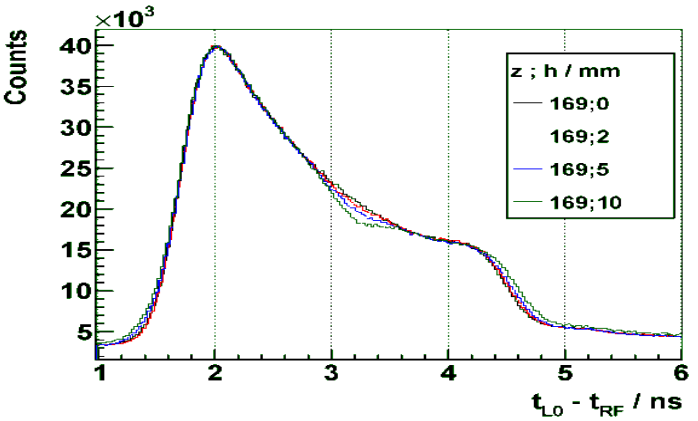


The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Prompt gamma timing

Gamma emission time is correlated with proton stopping time in the tissue, and thus with range.





Hueso González et al., PMB 60 (2015) 6247.

The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

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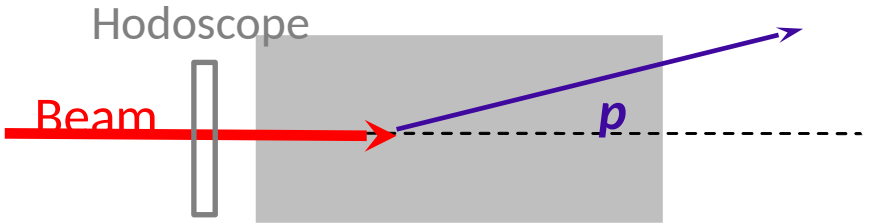
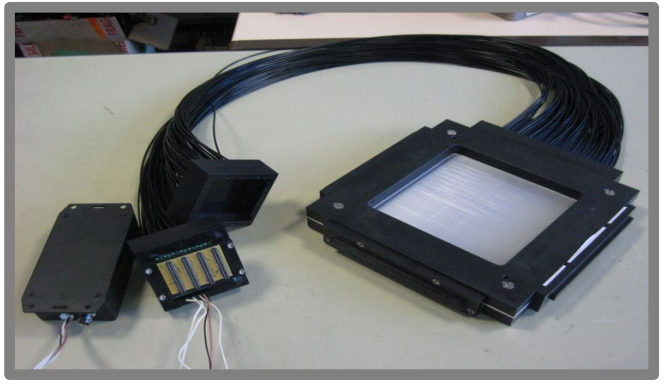
Hodoscopes



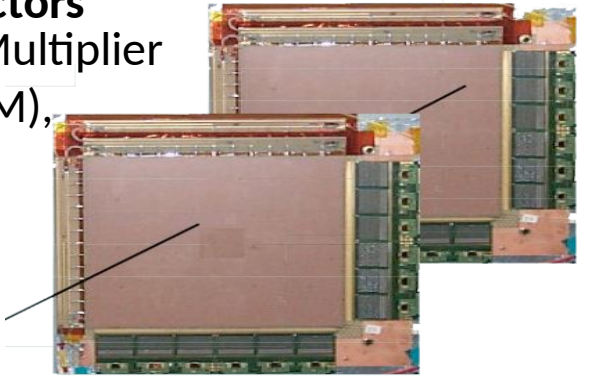
Silicon detectors: 4-plane proton tracker 2×2 cm^2.
12 µm Si-CMOS pixels , 50 µm thick ,

Plastic scintillators

Scintillating fibers
128 +128 fibers



Gaseous detectors
Gas Electron Multiplier chambers (GEM), 30x30 cm^2 active area



Diamond detectors

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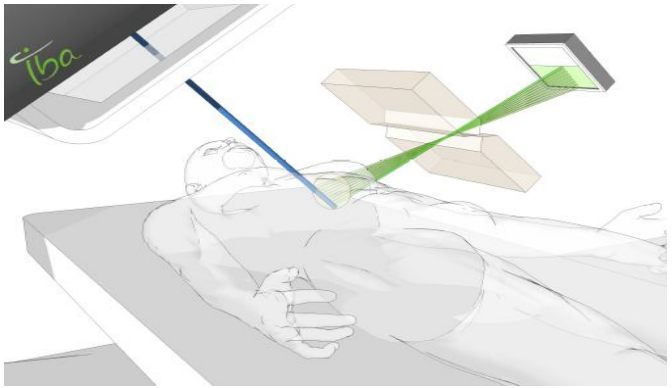
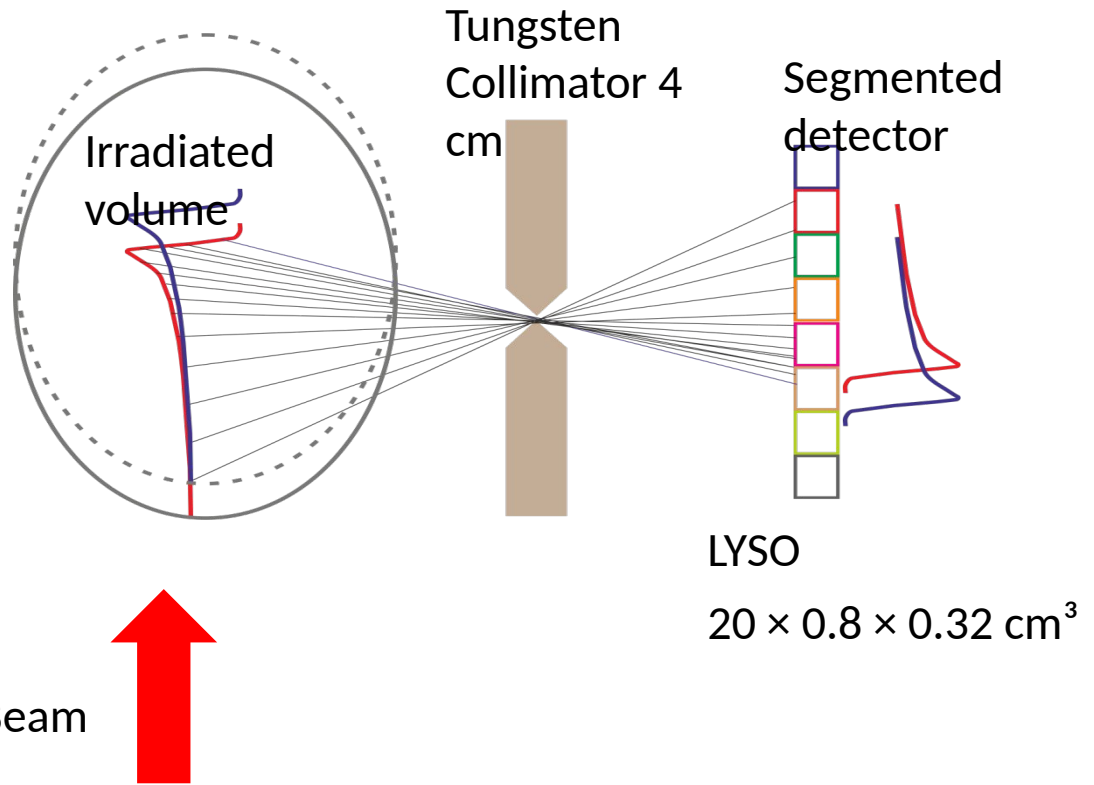
Prompt gamma imaging with collimated cameras



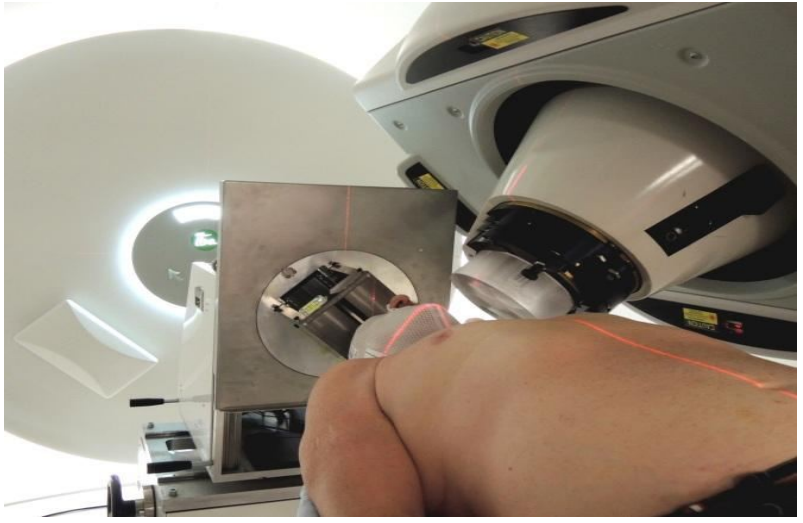


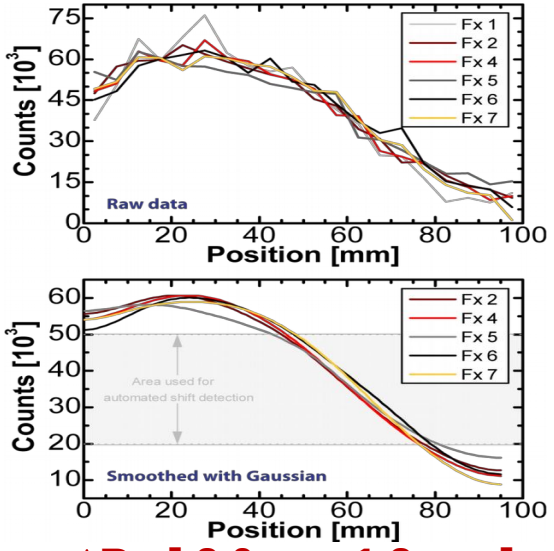
J. Smeets et al.: Phys. Med Biol. 57 (2012) 3371

The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Prompt gamma imaging with collimated cameras

- Range variations in the ~mm range have been observed.
- Successful results at therapeutic doses.
- Large, heavy system.





ΔR= [-2.0 mm,1.3 mm]

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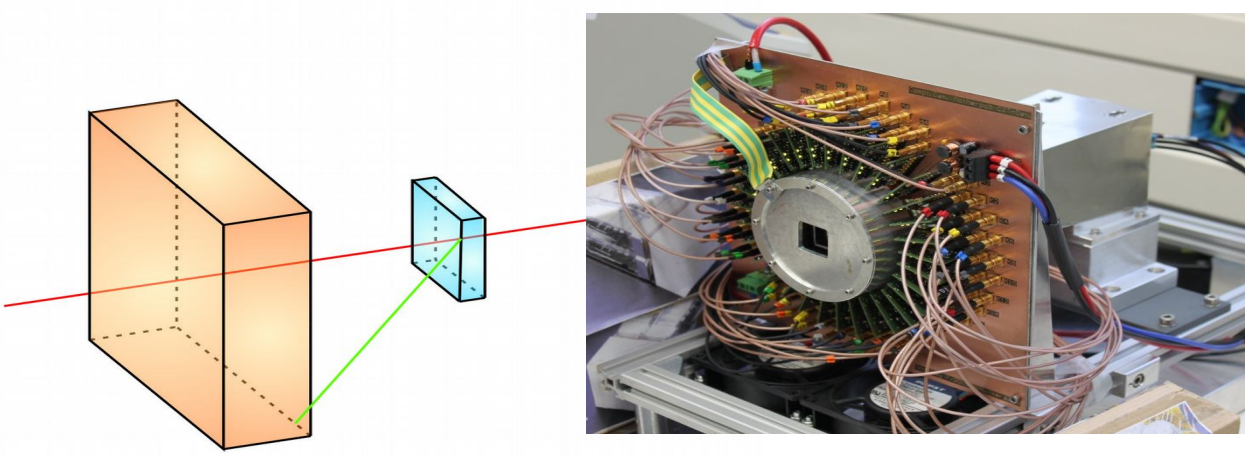
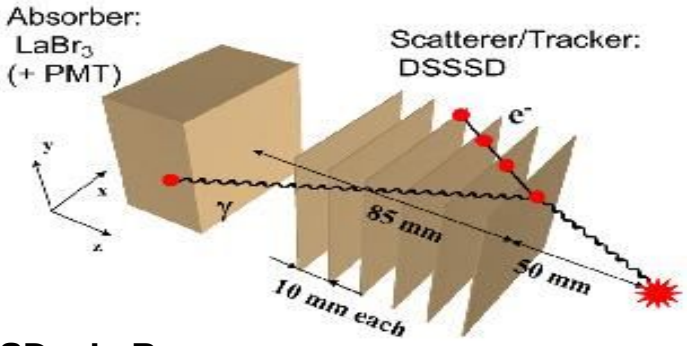
Prompt gamma imaging with Compton cameras

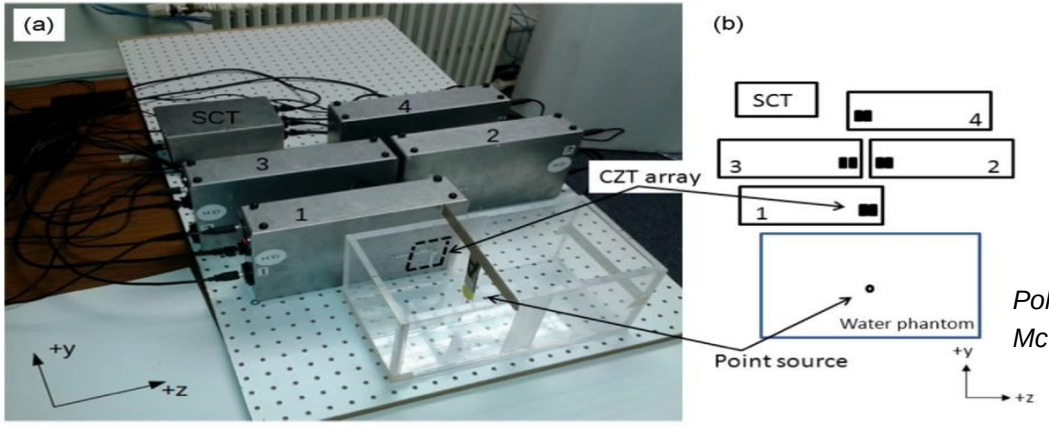
CZT + BGO



Thirolf et al., NN 2015



DSSD + $LaBr_3$



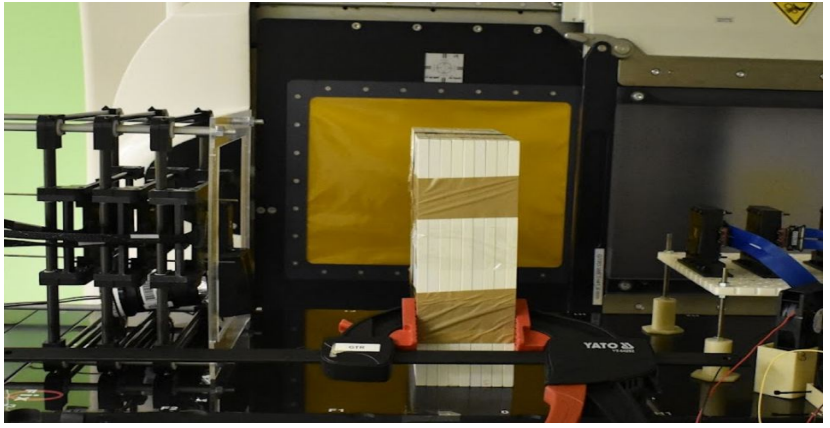
CZT

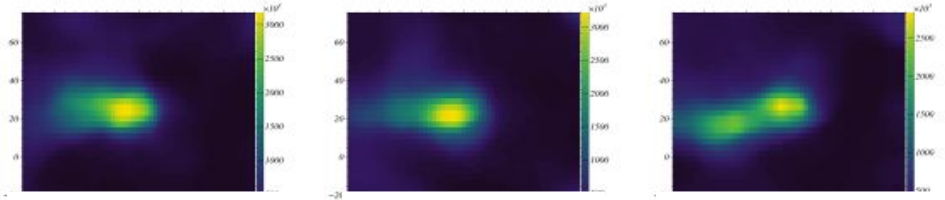
Polf et al., PMB 60 (2015) 7085
McCleskey et al., NIM A785 (2015) 163

The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Scintillator CCs

MACACO with $LaBr_3$ detectors

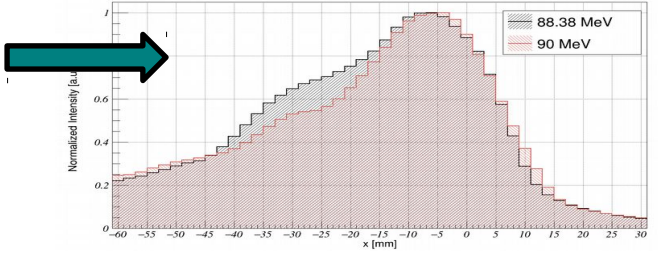




88.38 MeV 90 MeV 91.62 MeV

SiFi- CC: Compton camera with scintillating fibers under development

Proton beam at different energies



2 mm steps detected

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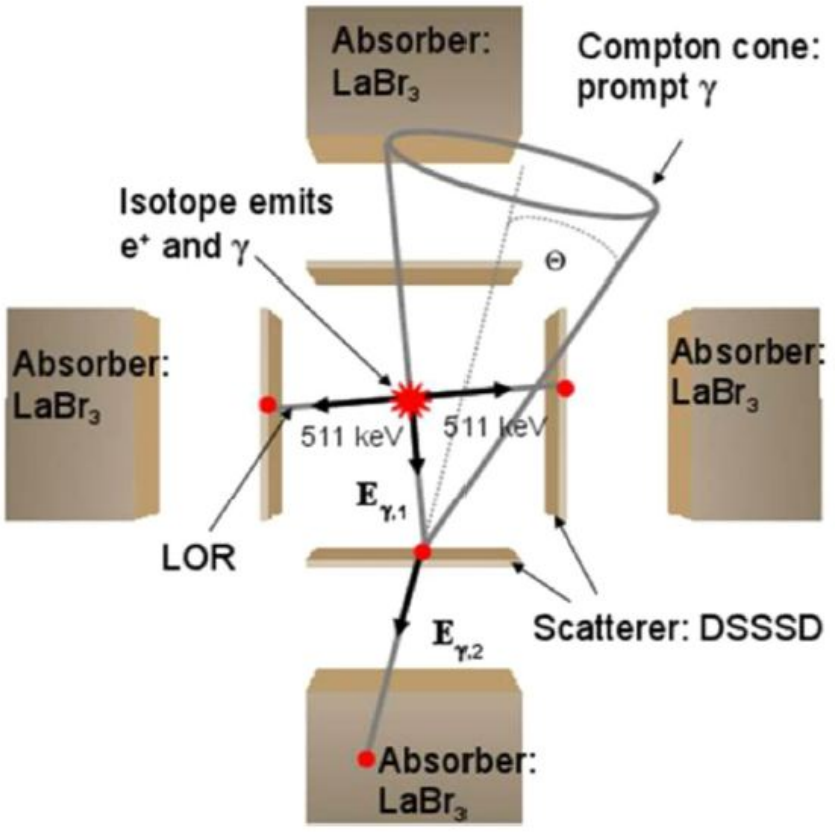
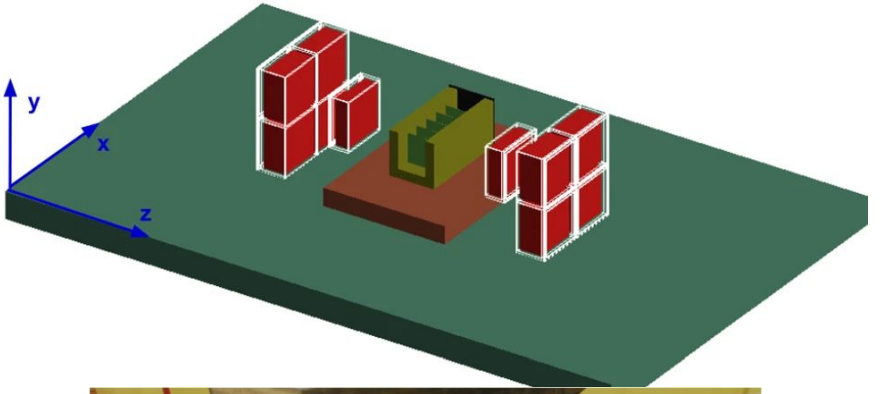
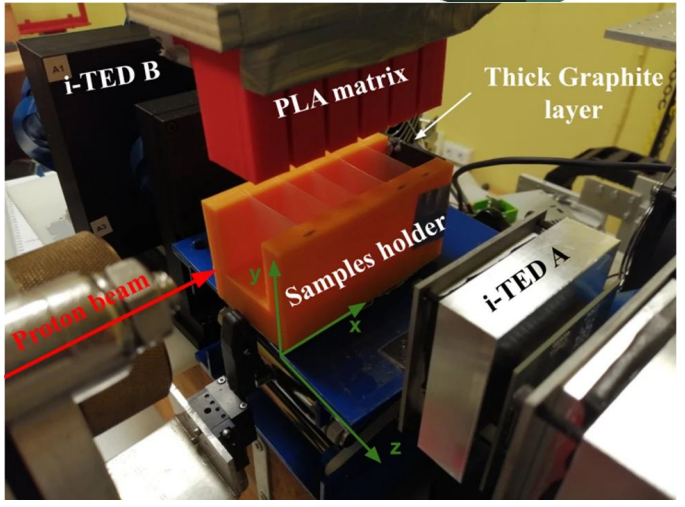
Combination Compton-PET



K. Parodi. NIM A 809 (2016) 113-119





J. Balibrea-Correa et al. Eur. Phys. J. Plus (2022) 137:1258

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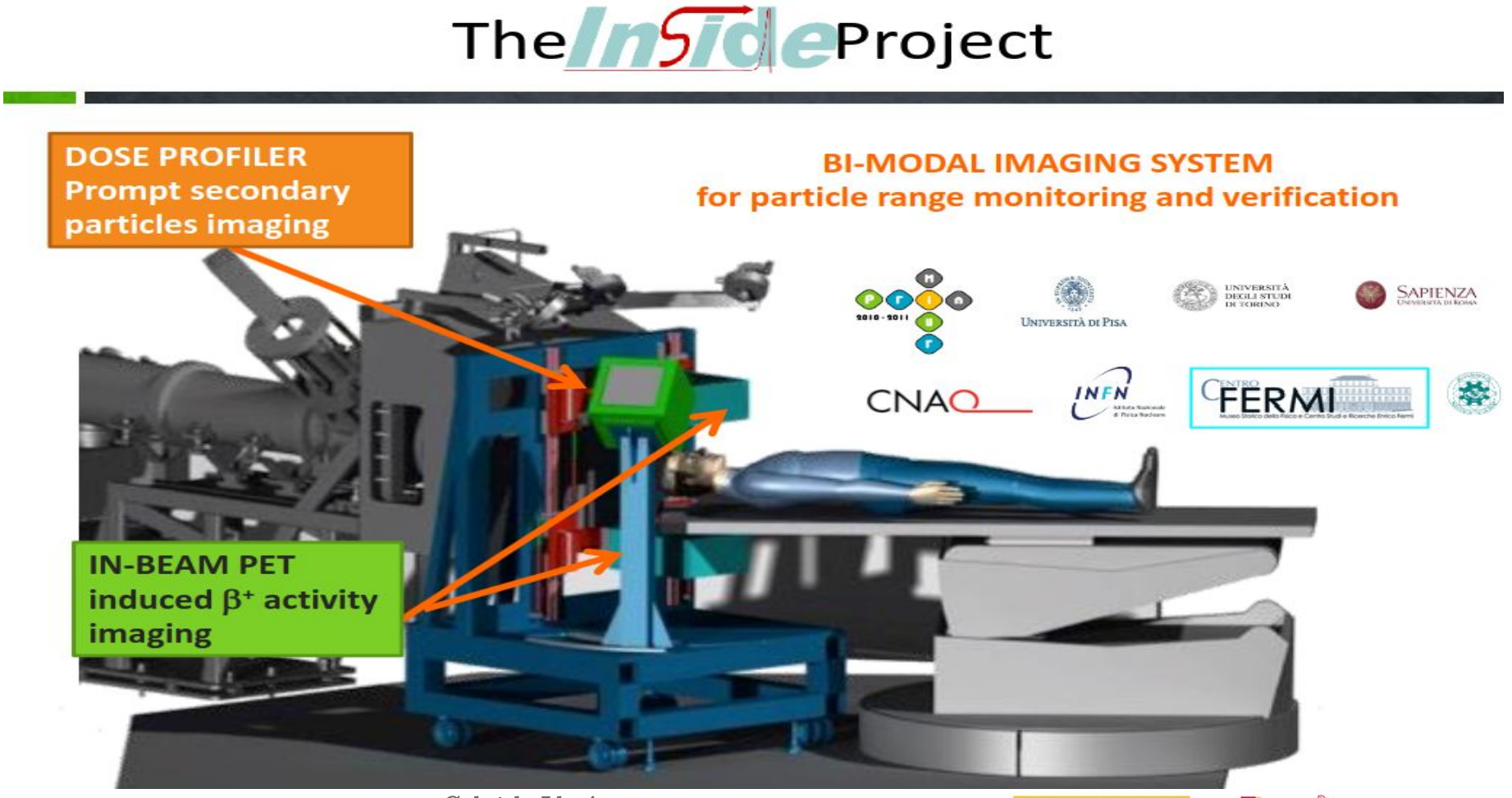
Inside project



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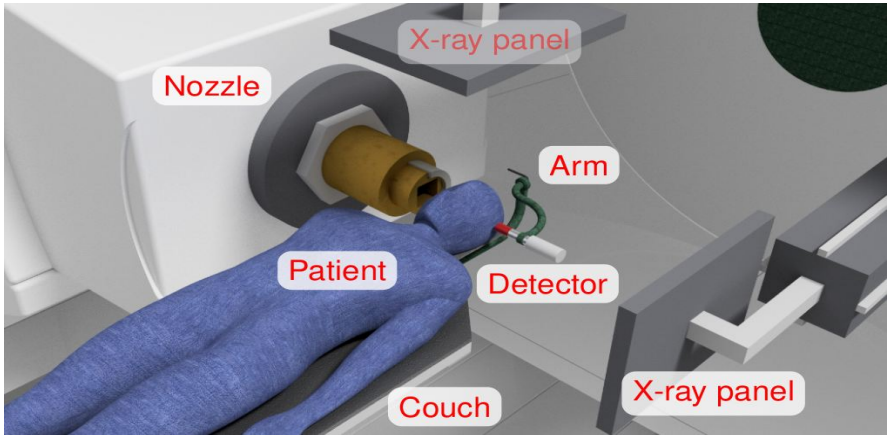
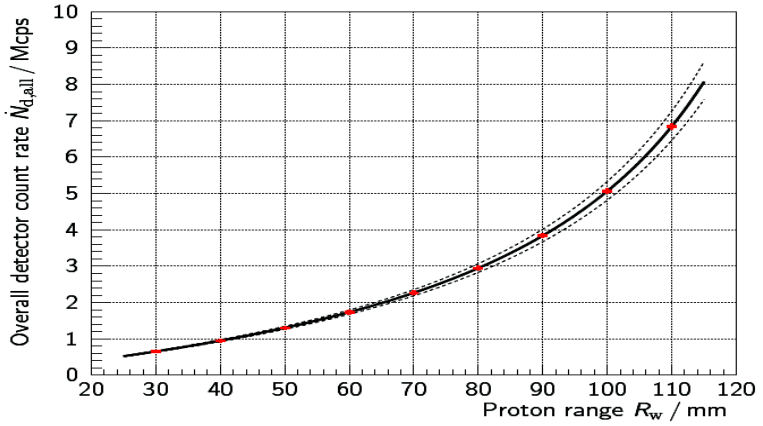
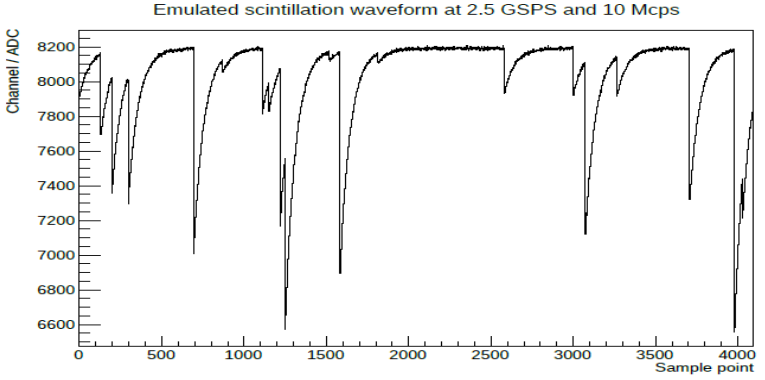
Coaxial Prompt gamma - ray monitoring





At 10 Mcps & 2.5 GSPS with a $CeBr_3$ detector, we expect (simulation):



- DAQ system working in raw-streaming mode (triggerless) with zero dead time
- Continuous streaming of full waveform during measurement (~30 s)
- Offline processing with pile-up reconstruction

F. Hueso-González et al.
2020, IEEE TRPMS 4-2.

Reduction of space, weight, channels and cost

The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Hadron therapy treatment monitoring

Unsolved problem

Challenging application

Even more challenging with modern synchrocyclotrons and flash (UHDR) therapy

Needs to be compatible with treatment

The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

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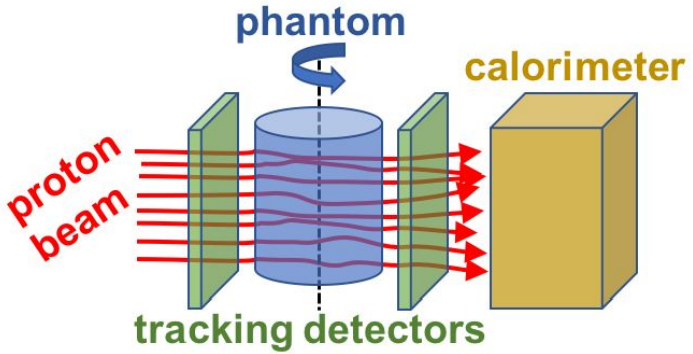
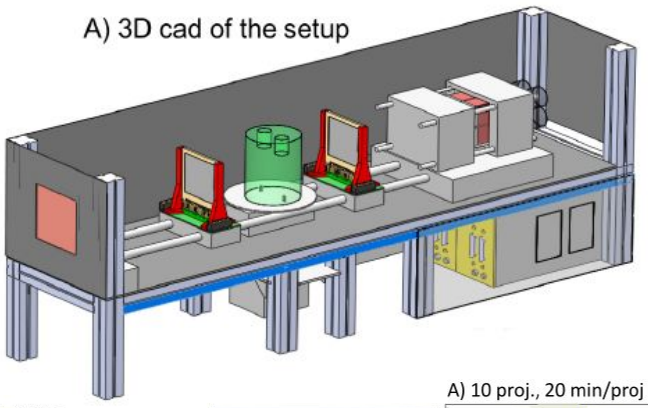
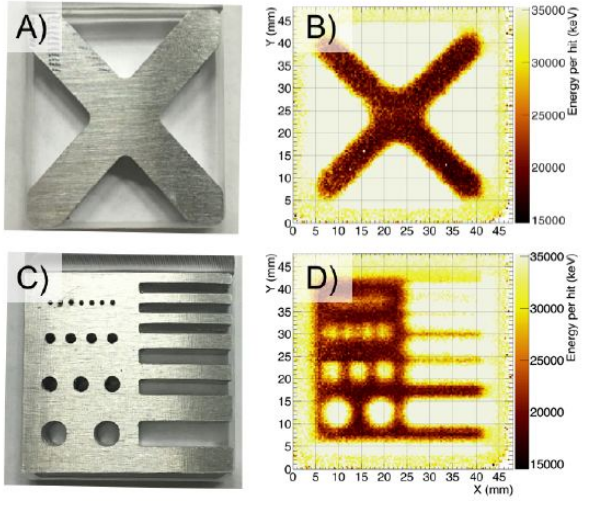
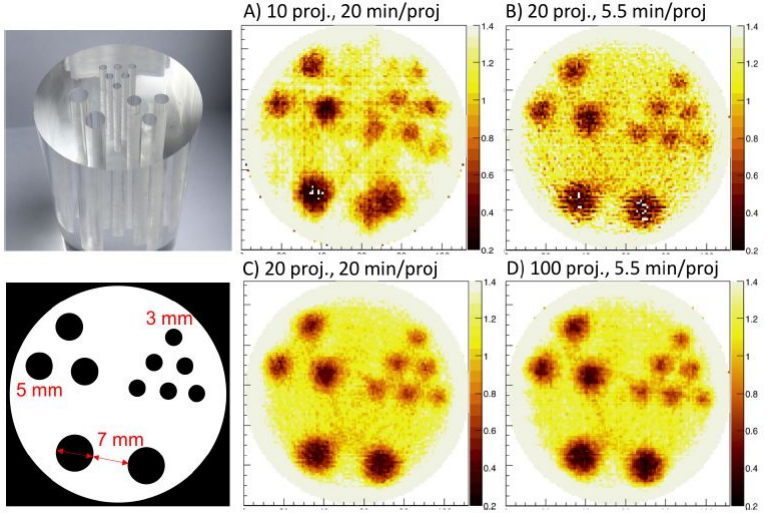
Proton radiography/tomography







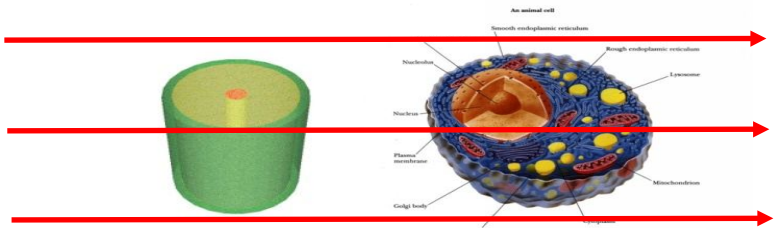


E. Nácher et al.
Eur. Phys. Jr.

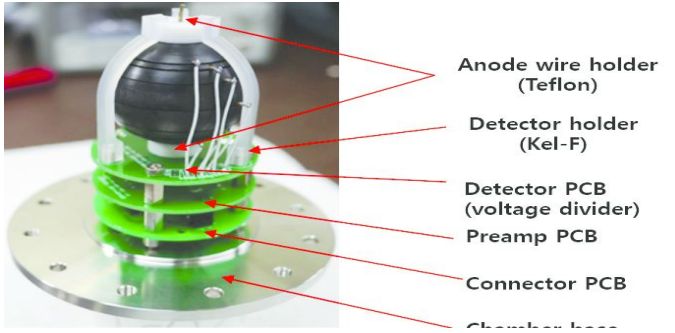
The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Microdosimetry

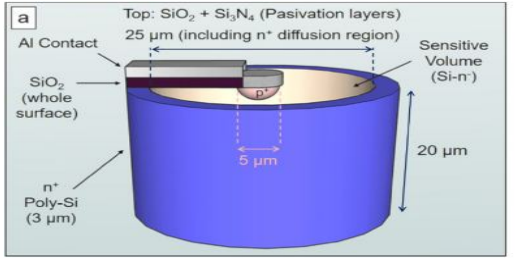
- Measurement of the energy deposition at the microscopic level.
- The measurement of the LET is important for the determination of the RBE, which is necessary for treatment planning and not well determined.
- TEPC (gaseous) microdosimeters were pioneers.
- Silicon and diamond are possible alternatives.

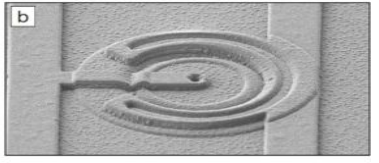


Microdosimeter (µm) **Cells**



- Size similar to cells.
- Low bias voltages.
- High resolution.
- Arrays of sensors to characterize the dose deposition along the protons' path.





LET – Linear Energy Transfer
RBE – Relative Biological Effectiveness
TEPC- Tissue Equivalent Proportional Counter

The ASFAE's research projects acknowledge the financial support from the MCIU with funding from the European Union NextGenerationEU and Generalitat Valenciana.

Conclusions

- Many aspects in which the performance of medical imaging devices can be improved.
- Instrumentation from astrophysics and HEP can lead to improvements in this field.
- Necessary contact with hospitals / specialized groups to know what the requirements are and to address properly the needs.

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Financiado por la Unión Europea NextGenerationEU
Gobierno de España · Ministerio de Ciencia, Innovación y Universidades
Plan de Recuperación, Transformación y Resiliencia
Generalitat Valenciana · Conselleria de Educación, Universidades y Empleo
GVA NEXT

Acknowledgements

- MCIU with funding from the European Union NextGenerationEU (PRTR-C17.I1) and Generalitat Valenciana. Proj. ICOR, ref. ASFAE/2022/019
- MCIU /AEI (PID2022-143246OB-I00).

Thank you

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