L International Meeting
on Fundamental Physics
and XV CPAN Days

2 — 6 October 2023

Palacio de la Magdalena · Santander (Spain)

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indico.cern.ch/e/IMFP-CPAN

Advances in medical physics from Nuclear and HEP

Gabriela Llosá

Instituto de física Corpuscular
(IFIC, CSIC-UV)

Outline

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

Medical imaging

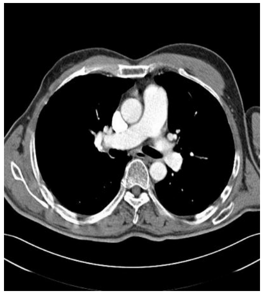
Discovery of X-rays: W. C. Röntgen, 1895.

→ **First Nobel Prize in physics, 1901.**

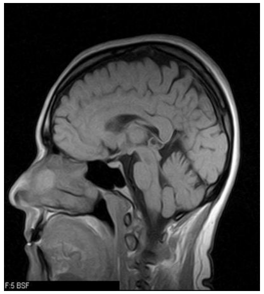
Medical imaging

Structural

CT

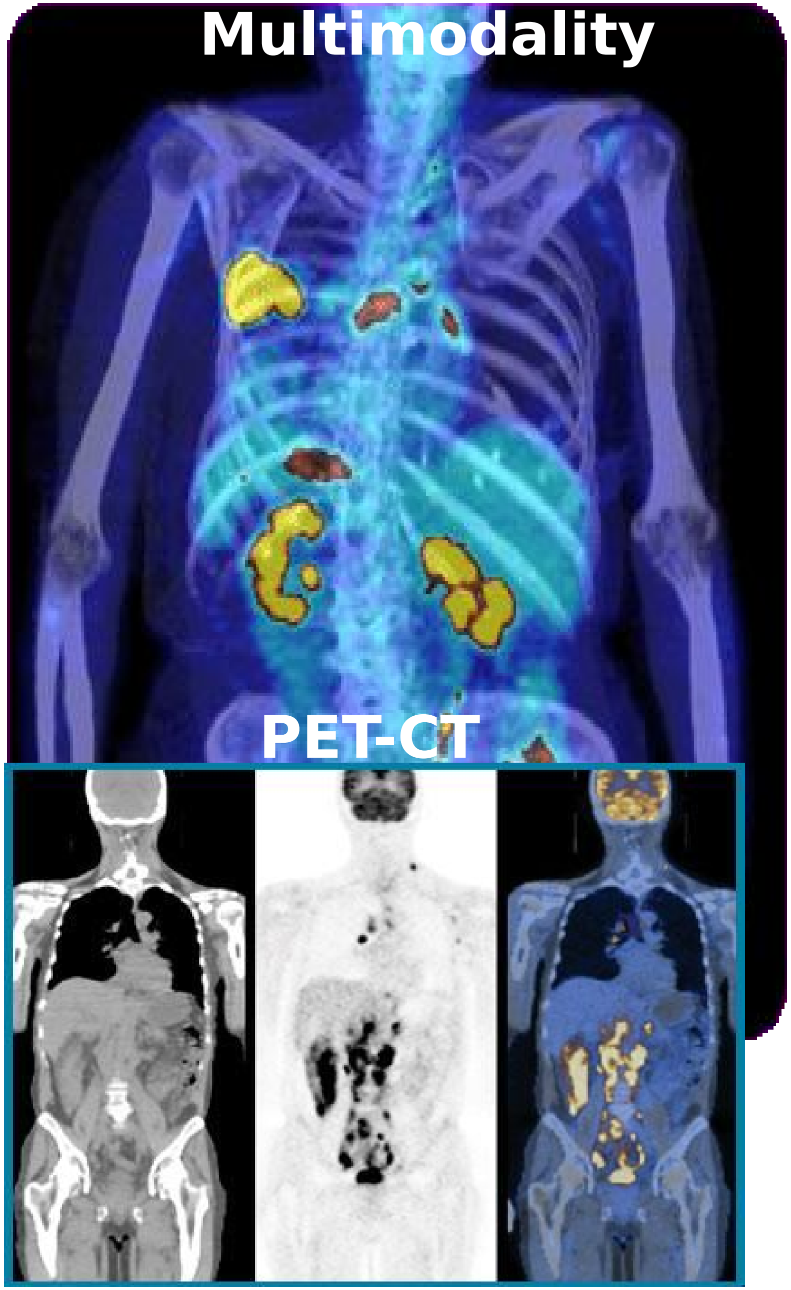


MRI



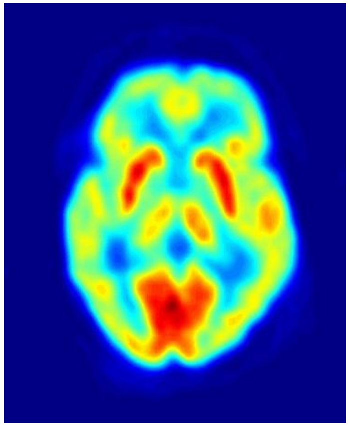
Ultrasounds

Multimodality



PET-CT

Functional



PET

SPECT

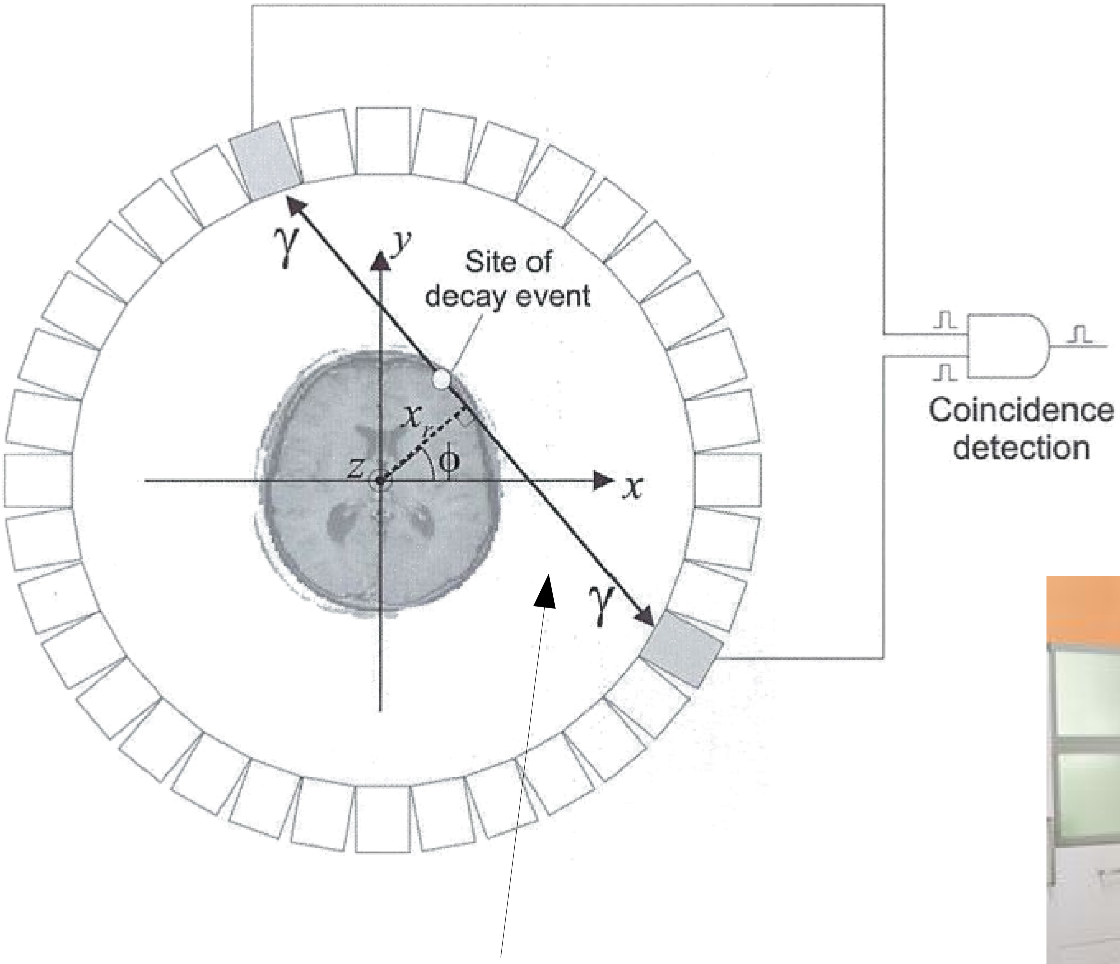
Goals

- Improve diagnostic accuracy
- Reduce dose / time

+ Lower cost

Positron Emission Tomography (PET)

Ring of detector heads

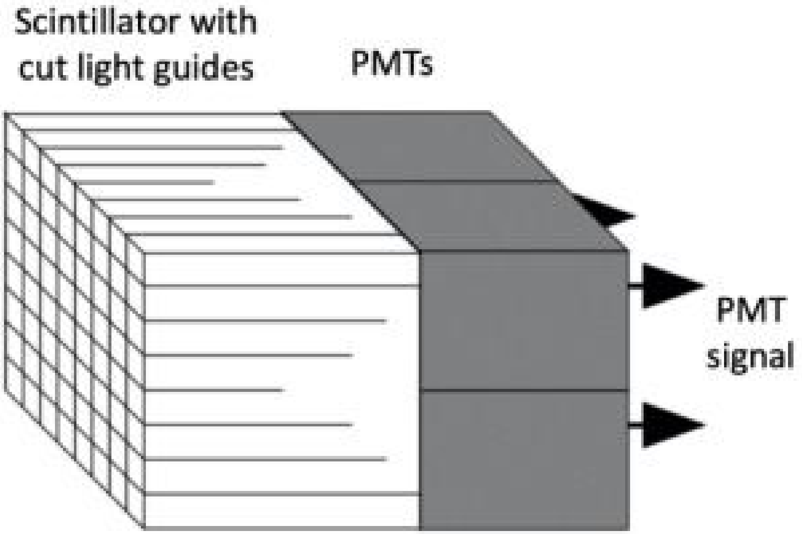


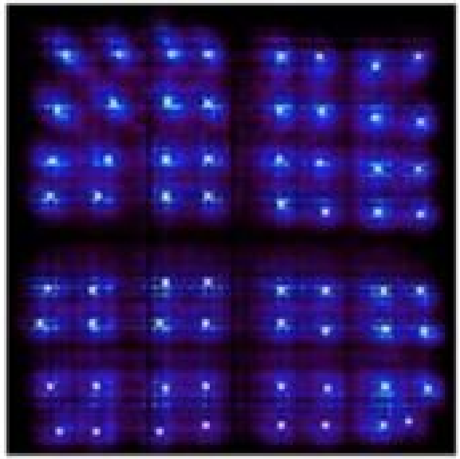
Line of response (LOR)

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

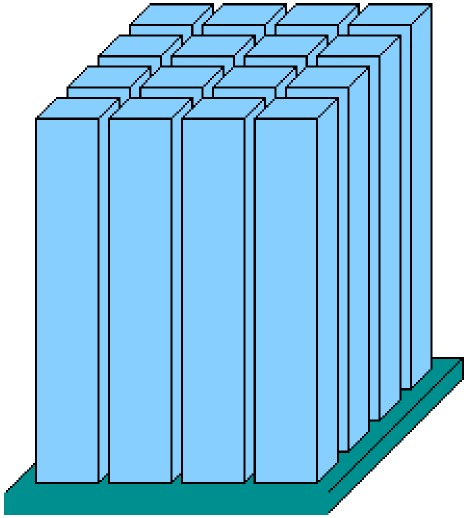
Philips Gemini TF PET/CT Scanner

PET - detectors





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



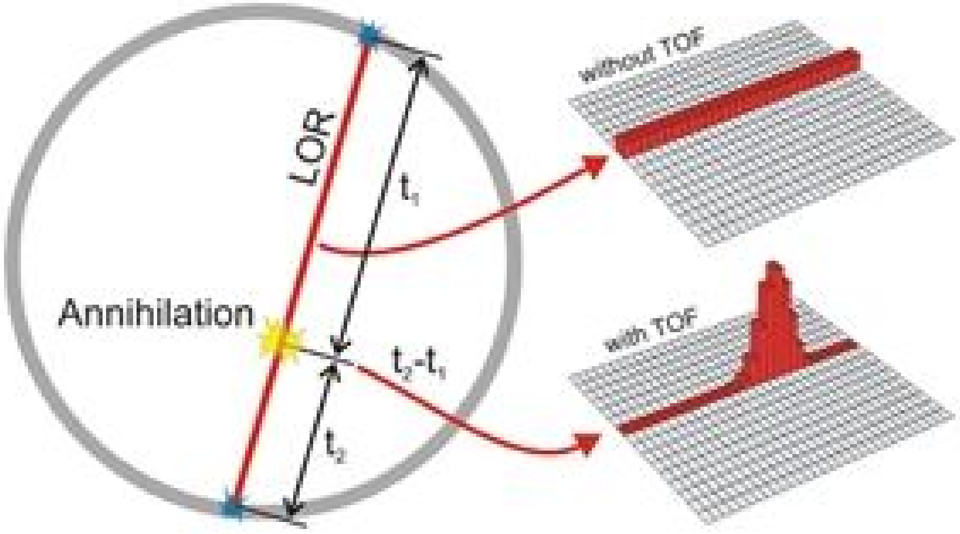
LSO / LYSO + SiPMs.
3-4 mm crystal size

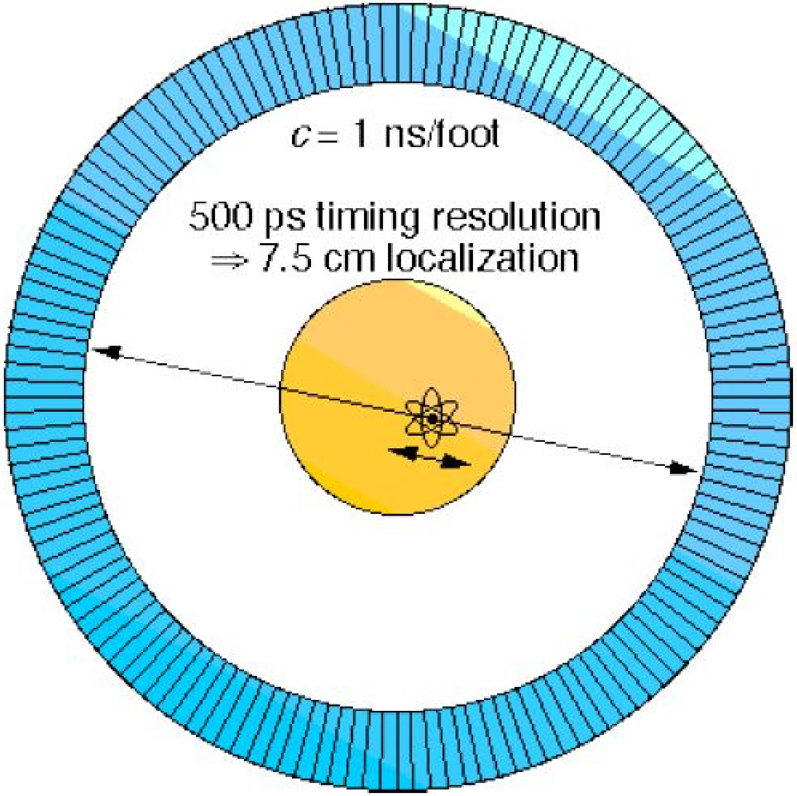
One-to-one coupling or
Multiplexing solutions
to reduce the number
of channels

(→ PET/MR)

Time-Of-Flight (TOF) PET

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



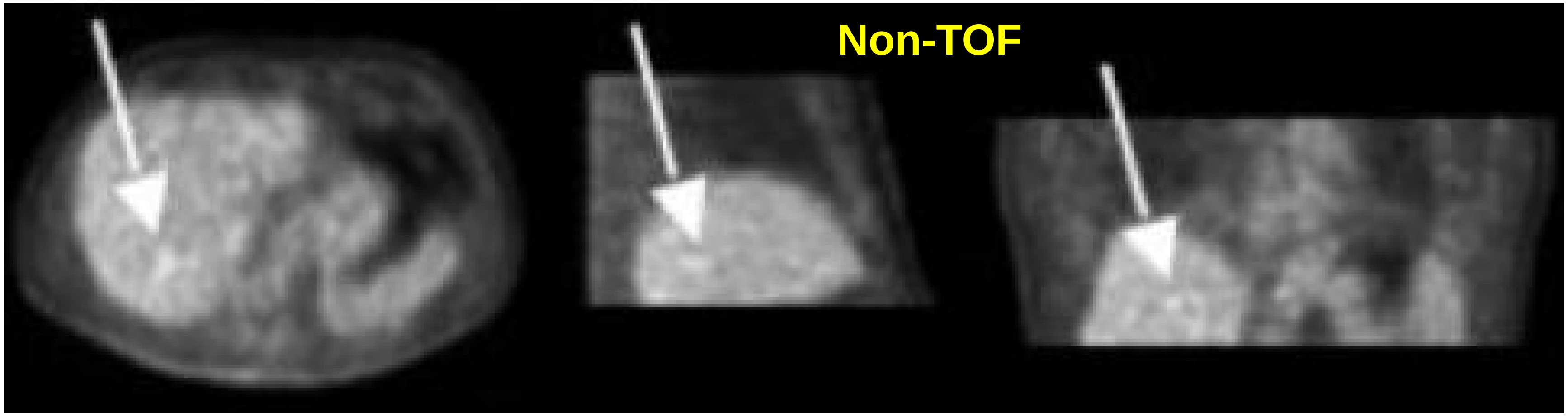


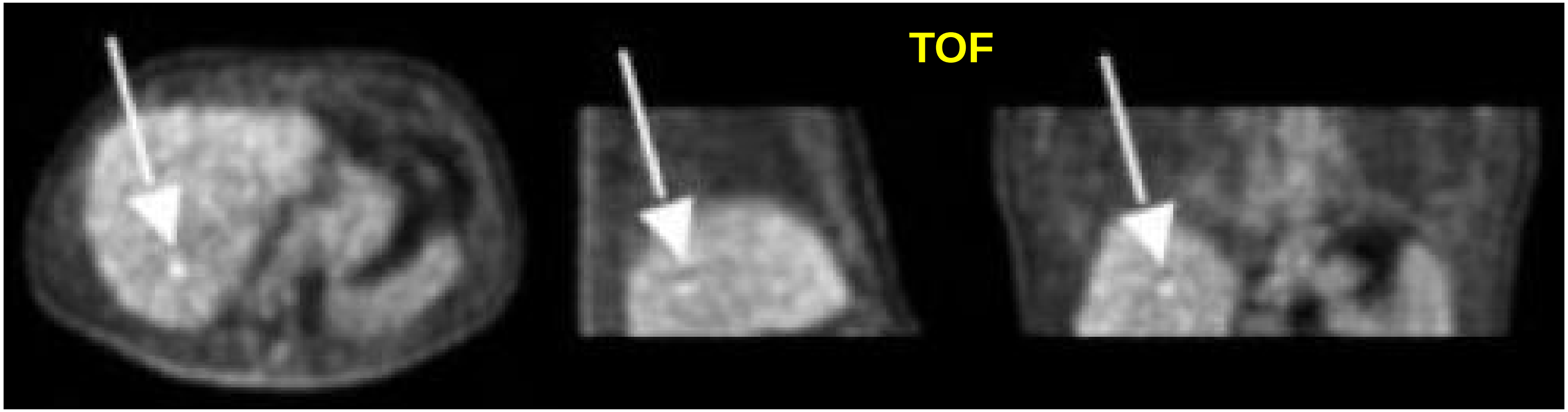
More accurate determination of the emission area of the photons → better signal-to-noise ratio (SNR).

TOF-PET first generation

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

TOF-PET

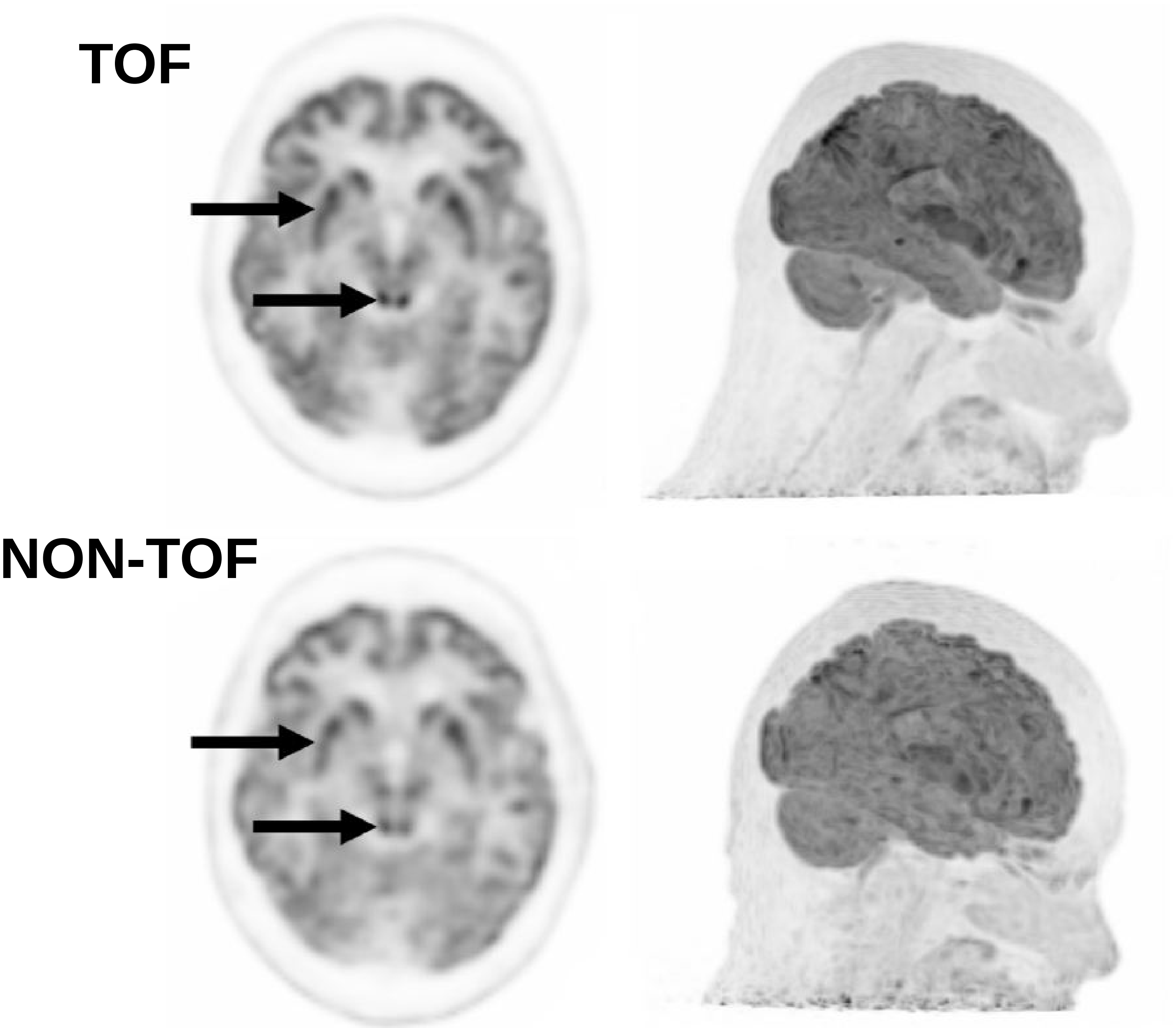




Liver lesion

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

TOF-PET

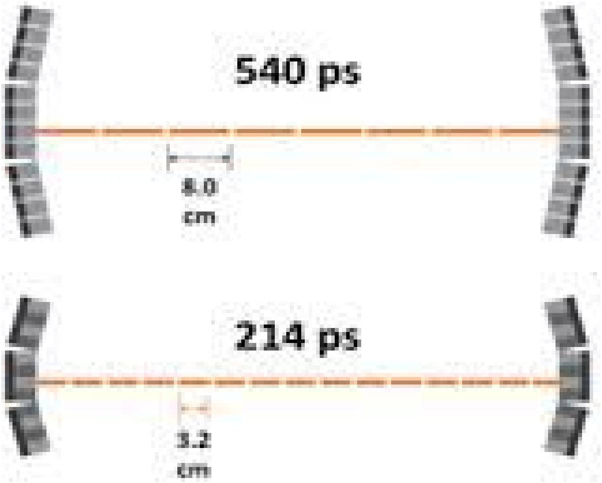


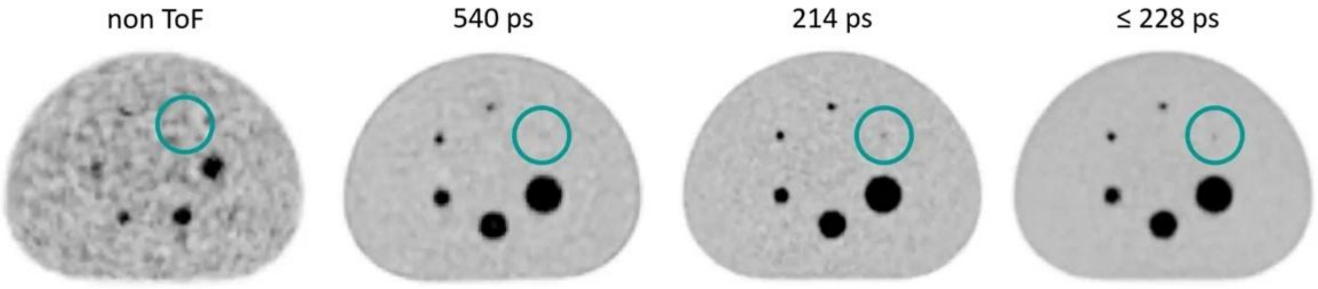
Van Sluis et al.

J Nuc Med 2019

TOF-PET

Last generation with SiPMs: 214-380 ps FWHM



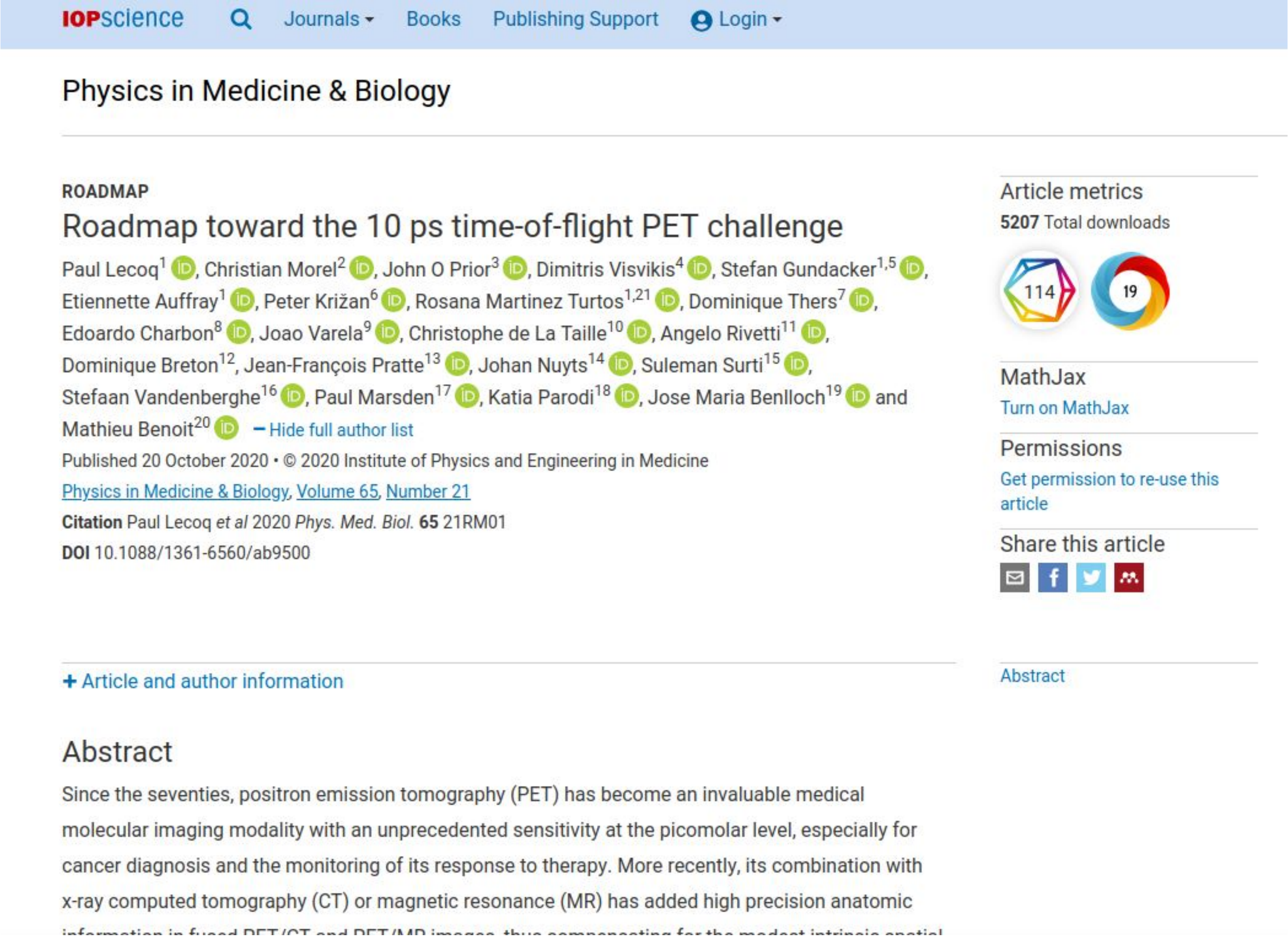


Sphere size (mm): 5, 8, 10, 13, 28, 37; 4:1 CBR

Siemens Biograph Vision: 214 ps.

TOF-PET

The 10 ps challenge → 1.5 mm LOR



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

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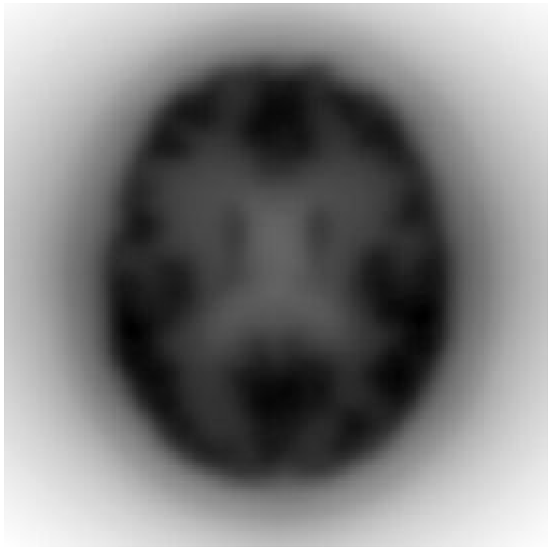
Abstract

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 information in fused PET/CT and PET/MR images, thus compensating for the modest intrinsic spatial

Non-TOF



TOF 10 ps

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

TOF-PET

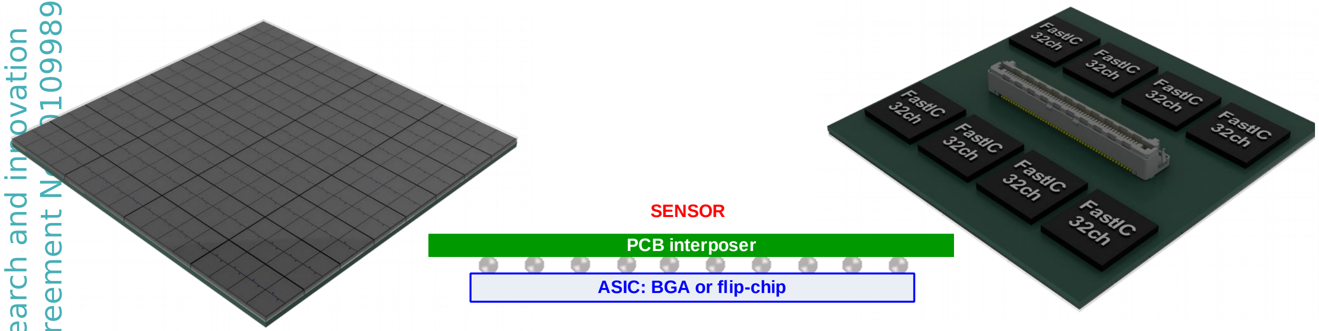
Next generation limited-angle time-of-flight PET imager

http://petvision.org

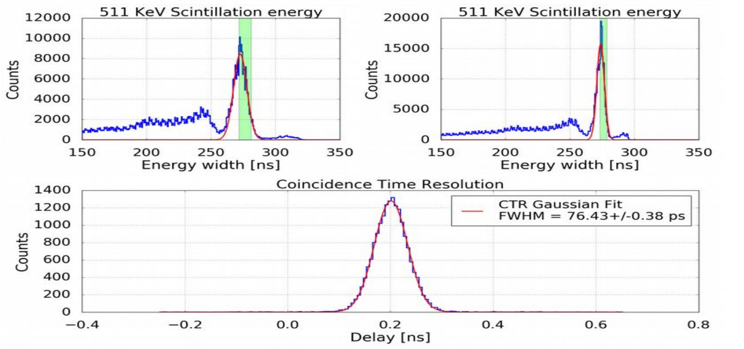
Funded by the European Union

This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement N 01099896

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

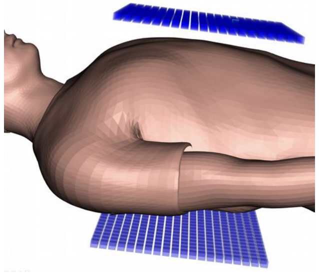


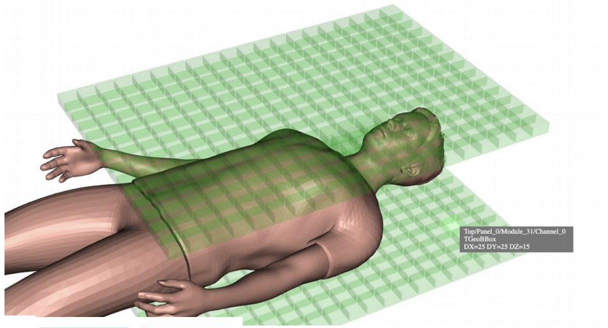
Preliminary results (non-integ. sensor)



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

Enable limited angle and affordable total body devices





Institut "Jožef Stefan" Ljubljana, Slovenija

FONDAZIONE BRUNO KESSLER FUTURE BUILT ON KNOWLEDGE

ICCUB

Institut de Ciències del Cosmos UNIVERSITAT DE BARCELONA

i3M Instituto de Instrumentación para Imagen Molecular

ONCO VISION

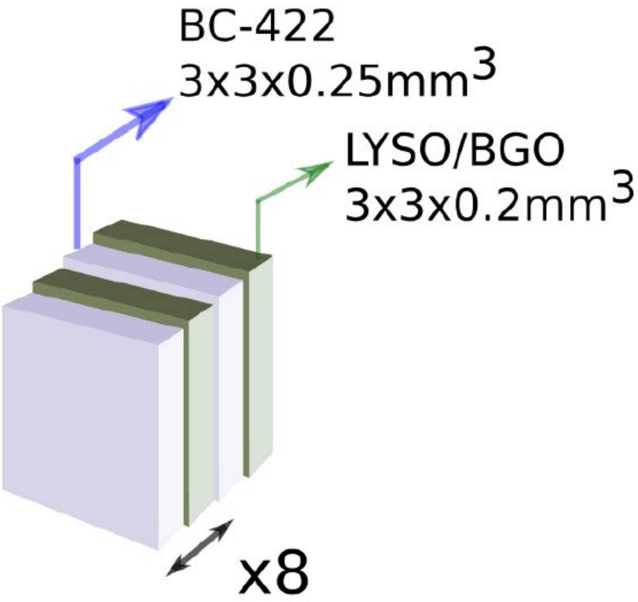
MGH 1811

Klinikum rechts der Isar Technische Universität München

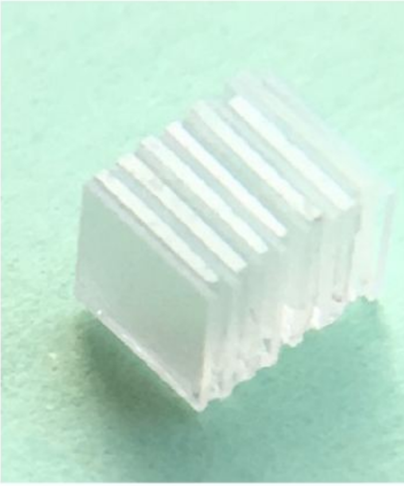
Courtesy of Rok Pestotnik

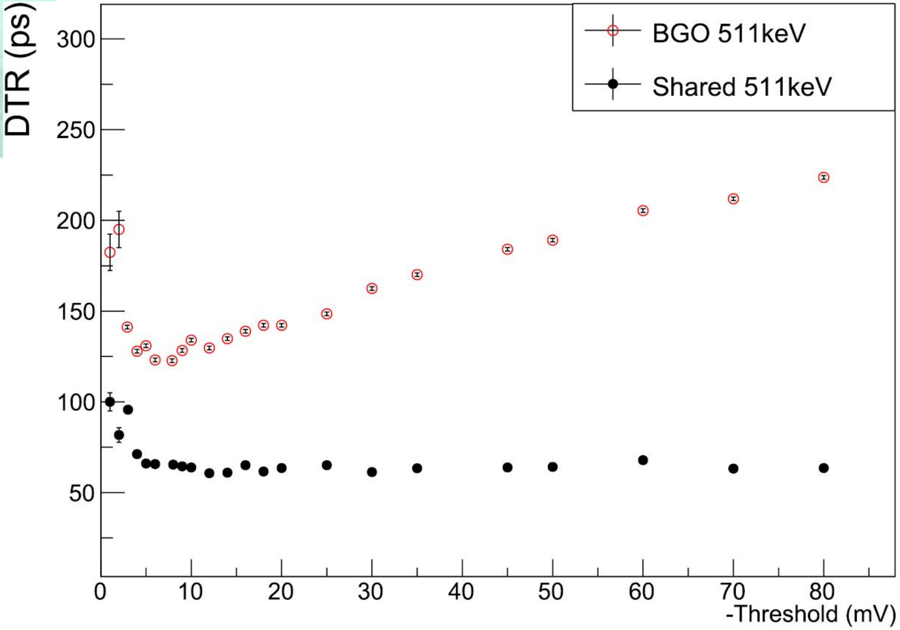
TOF-PET

New materials / metamaterials.



BGO + BC-422
sampling pixel

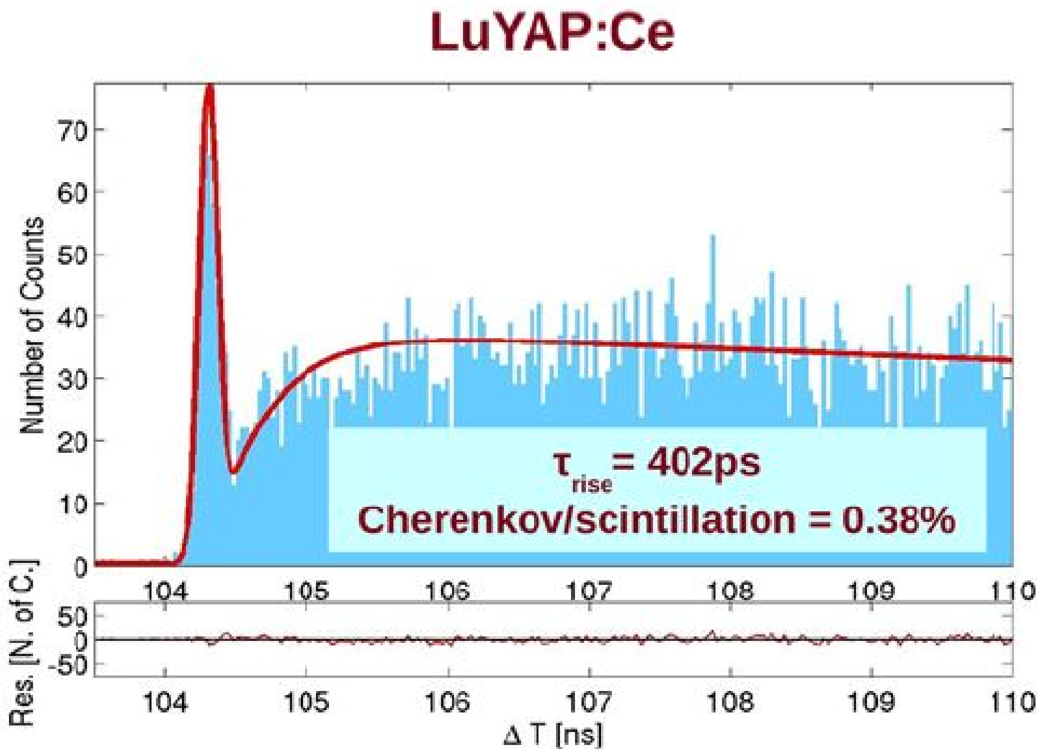




R M Turtos et al. Phys. Med. Biol. 2019

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

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

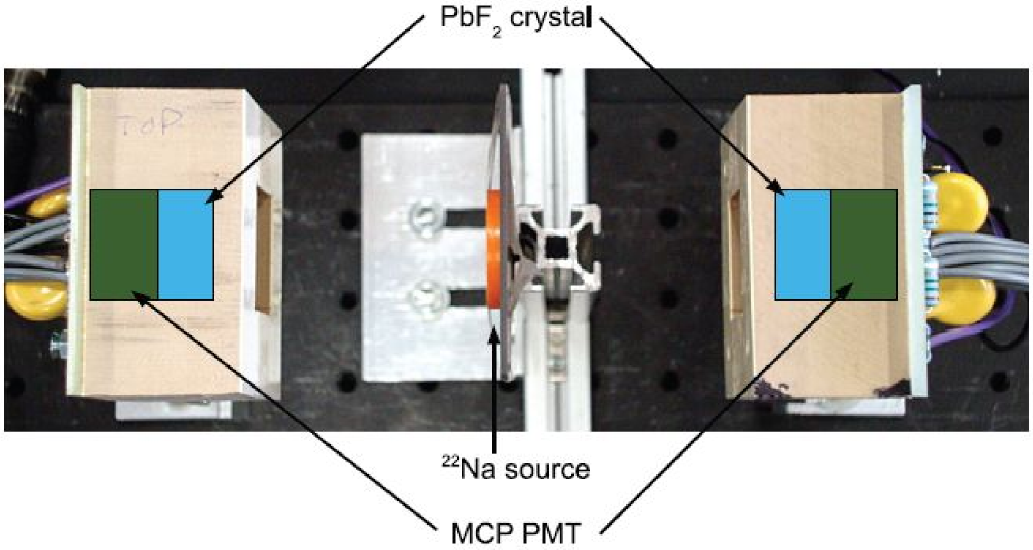


Fig. 1. The experimental setup with ^{22}Na source in between the two PbF_2 crystals coupled to MCP PMTs.

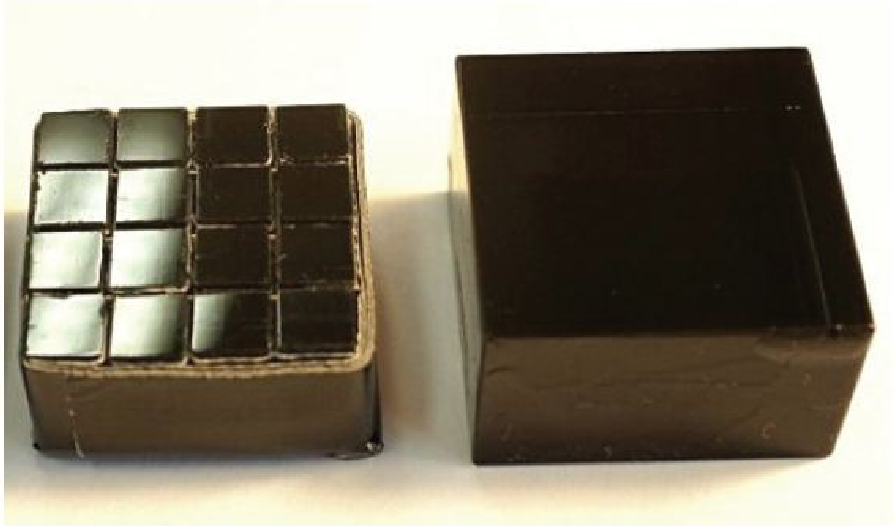
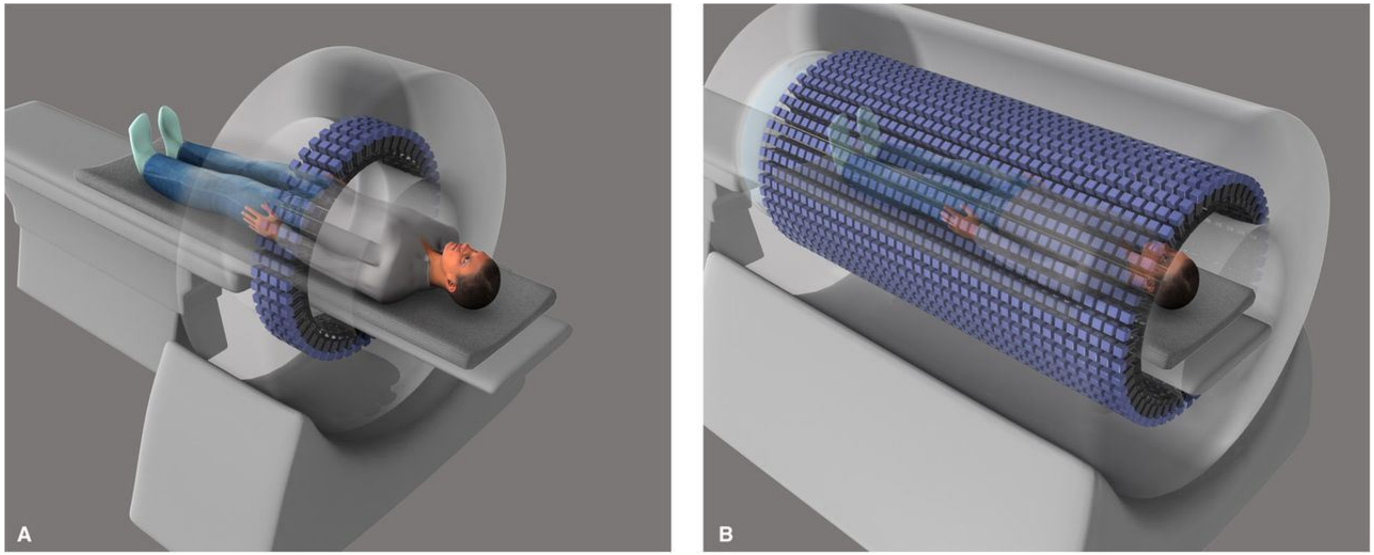
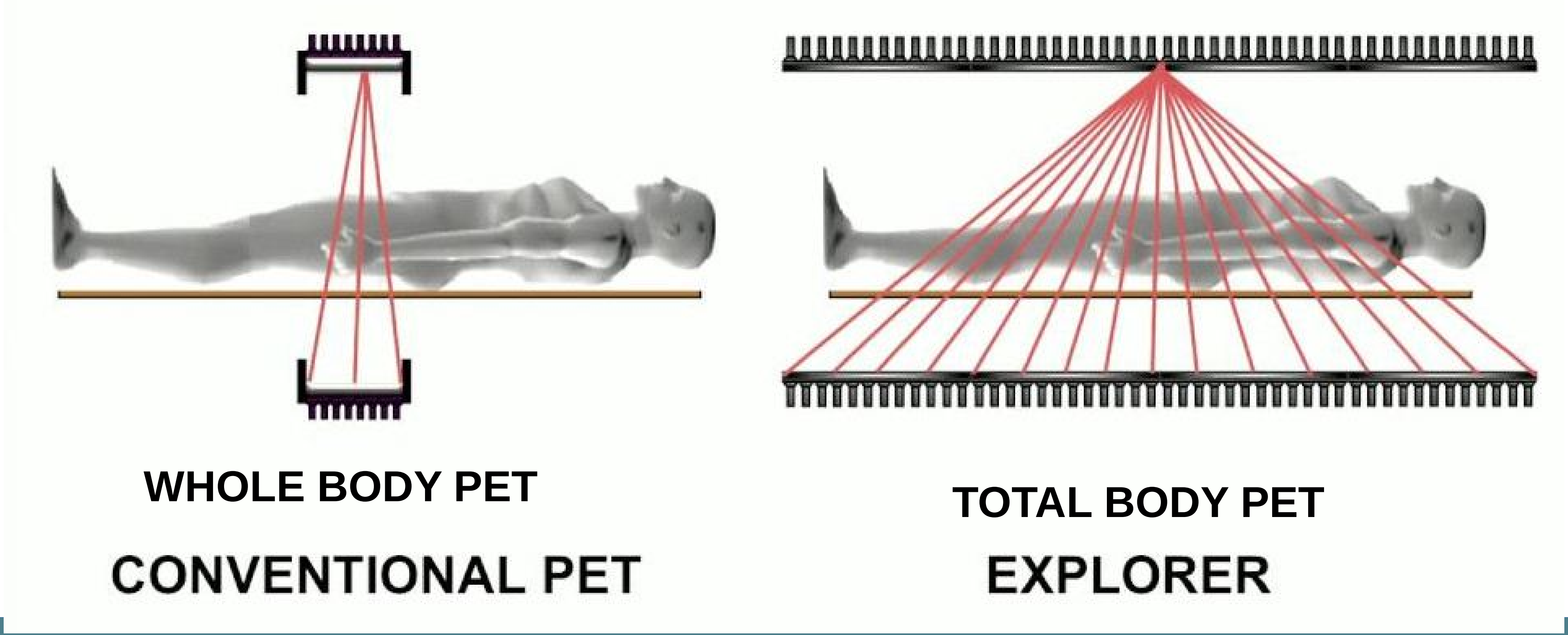


Fig. 2. Cherenkov radiator crystals used for detection of 511 keV photons in the present experiment.

Total Body PET

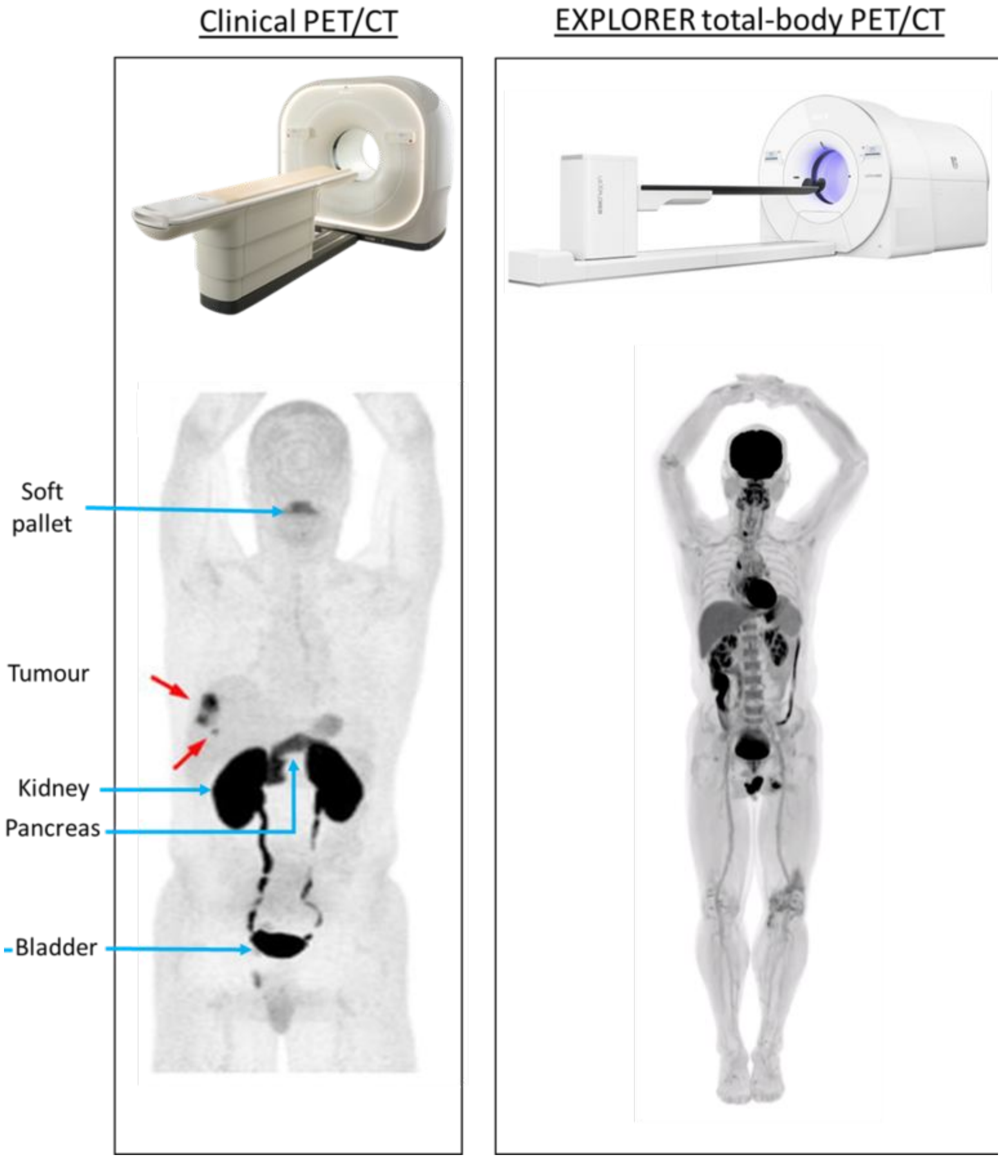




WHOLE BODY PET

TOTAL BODY PET

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.

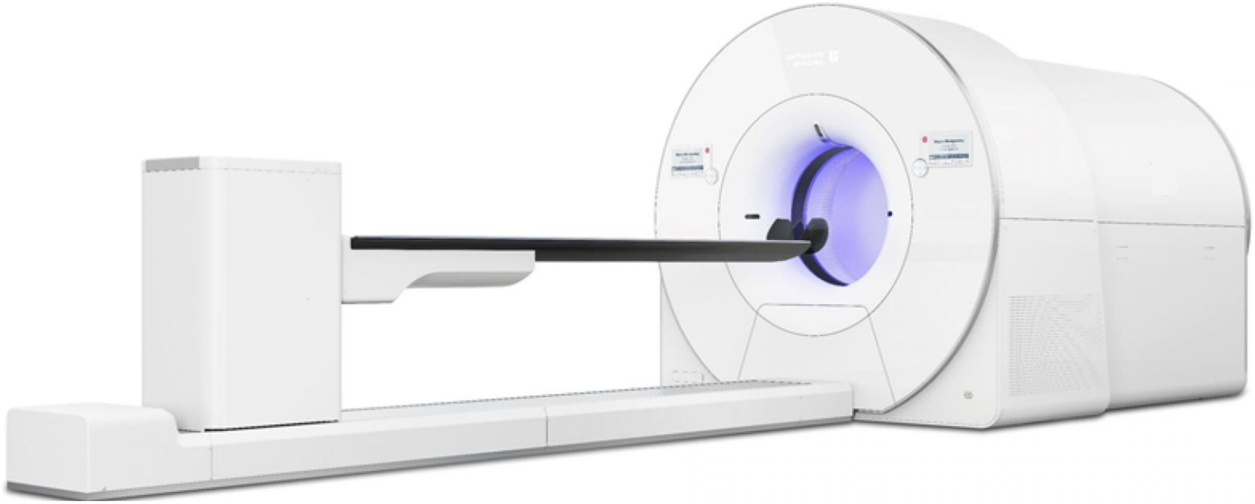
- Possibility of acquiring images furing longer time (reveral radiotracer half lives)

  → Kinetic studies and dynamic images.

- Umprecedented quality.

☹ Very high cost

Total Body PET

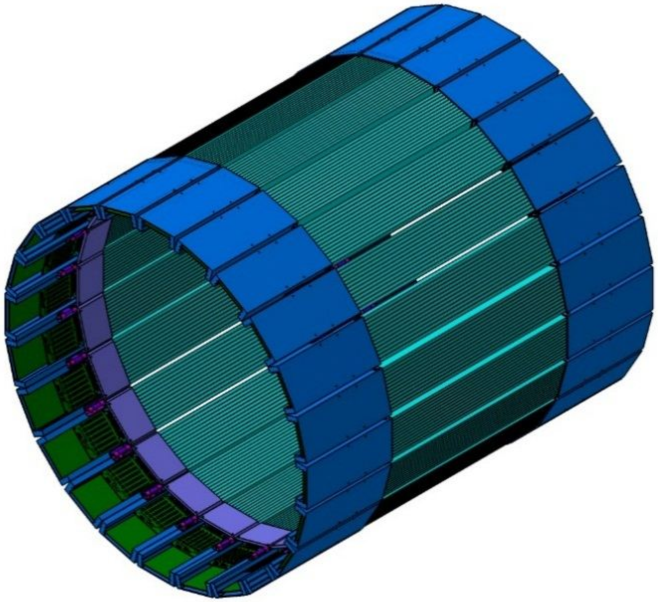


EXPLORER
Whole body length

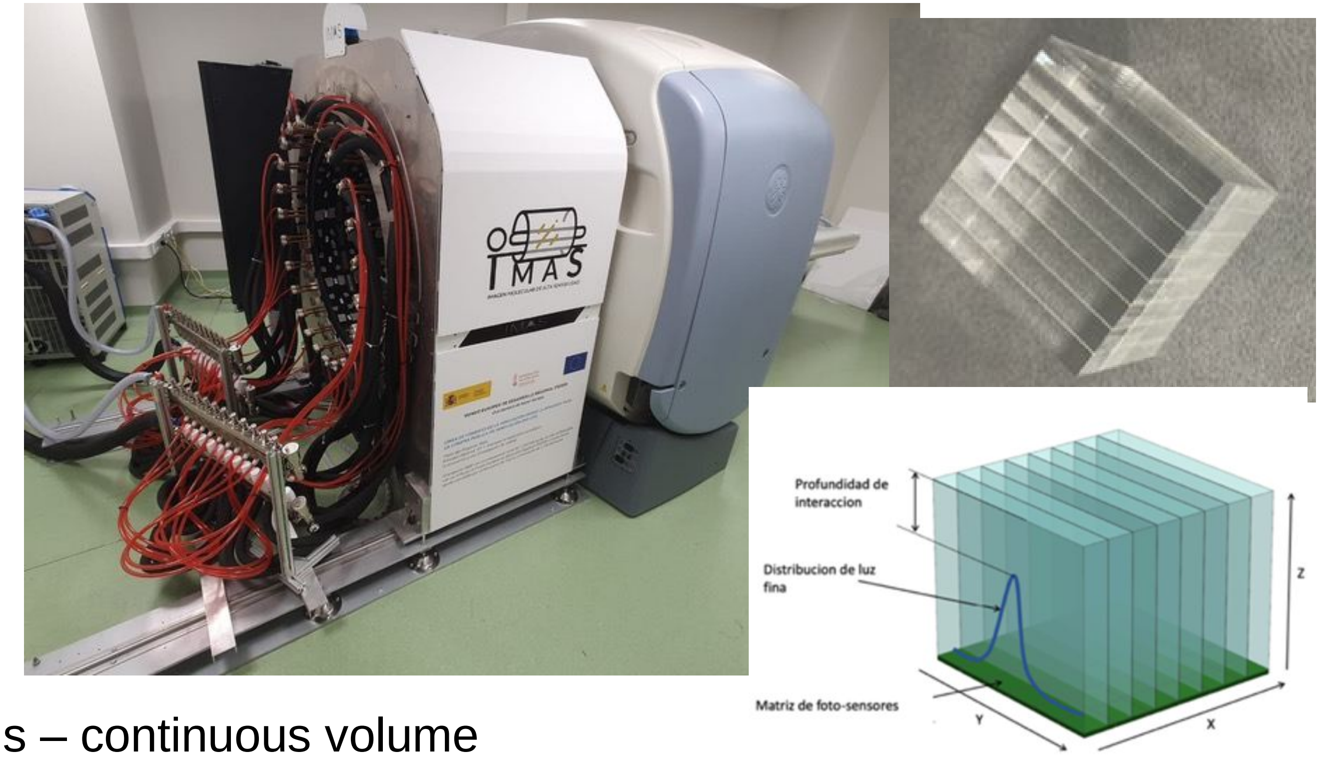
Biograph Vision Quadra
1 m length

Total Body PET – affordable approaches

JPET: plastic scintillators
+ trigerless acquisition

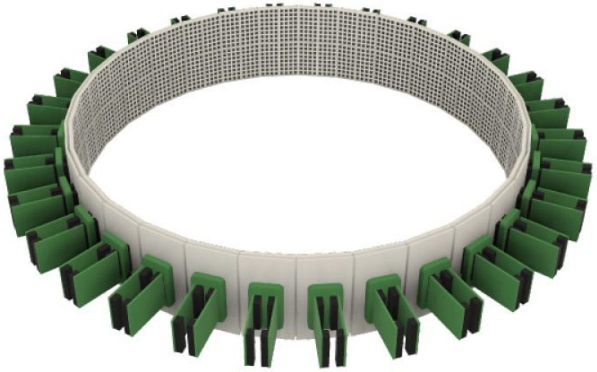


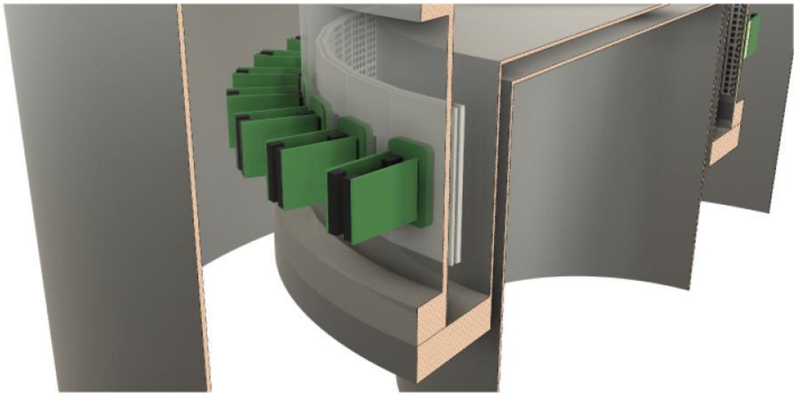
IMAS: semi-monolithic LYSO detectors



Courtesy of A. González

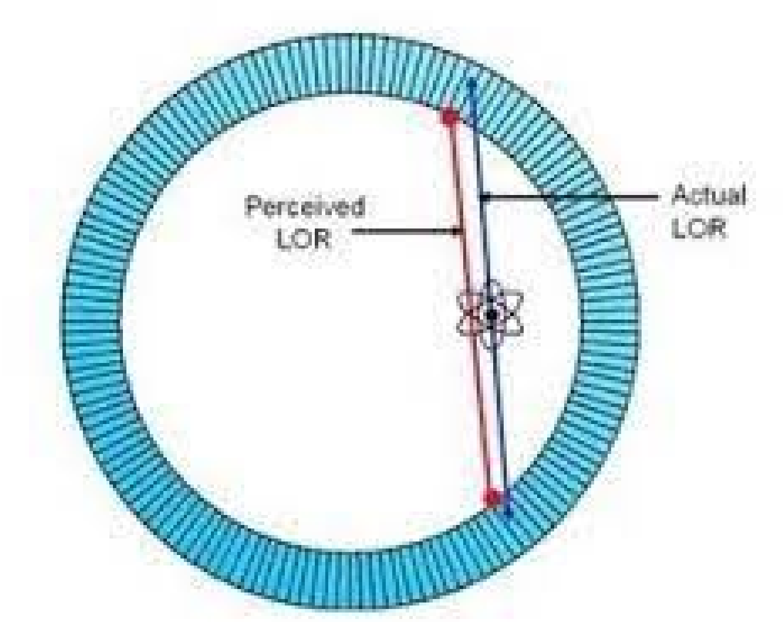
PETALO: liquid Xenon + SiPMs – continuous volume



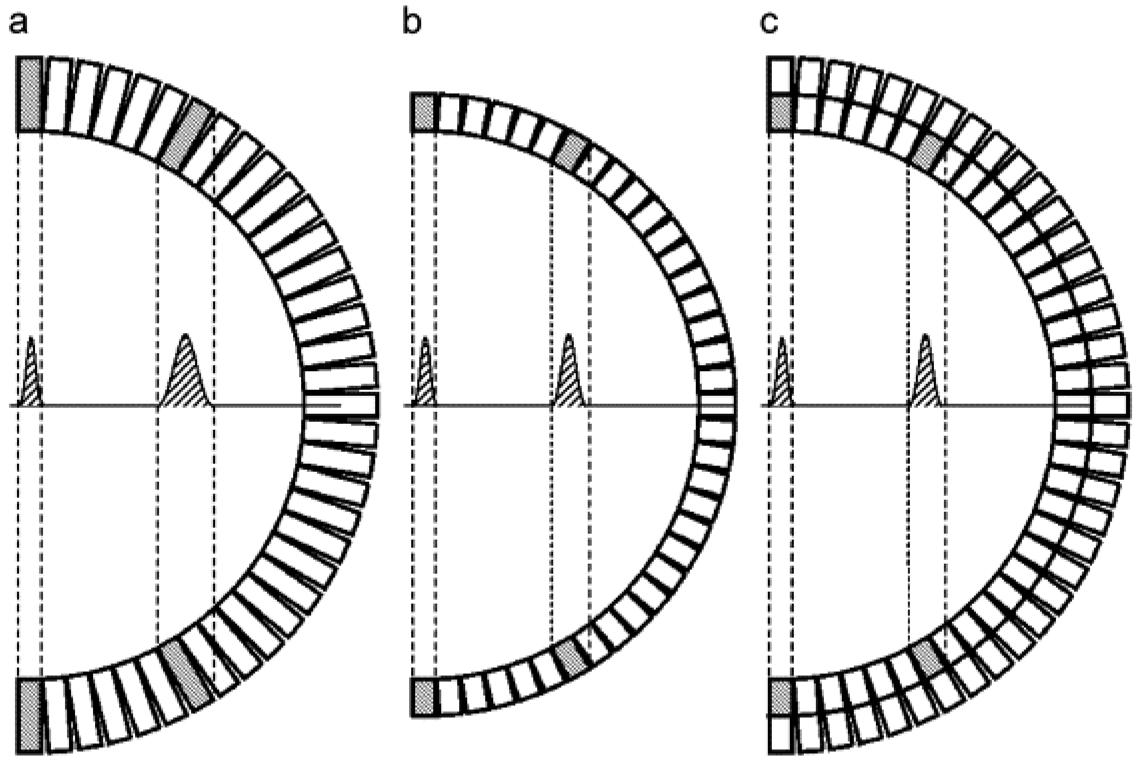


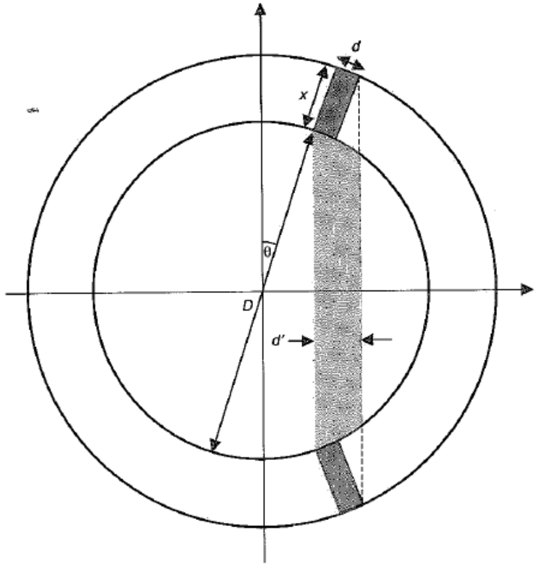
Again BGO?
Other?

Depth-of-Interaction (DOI) determination

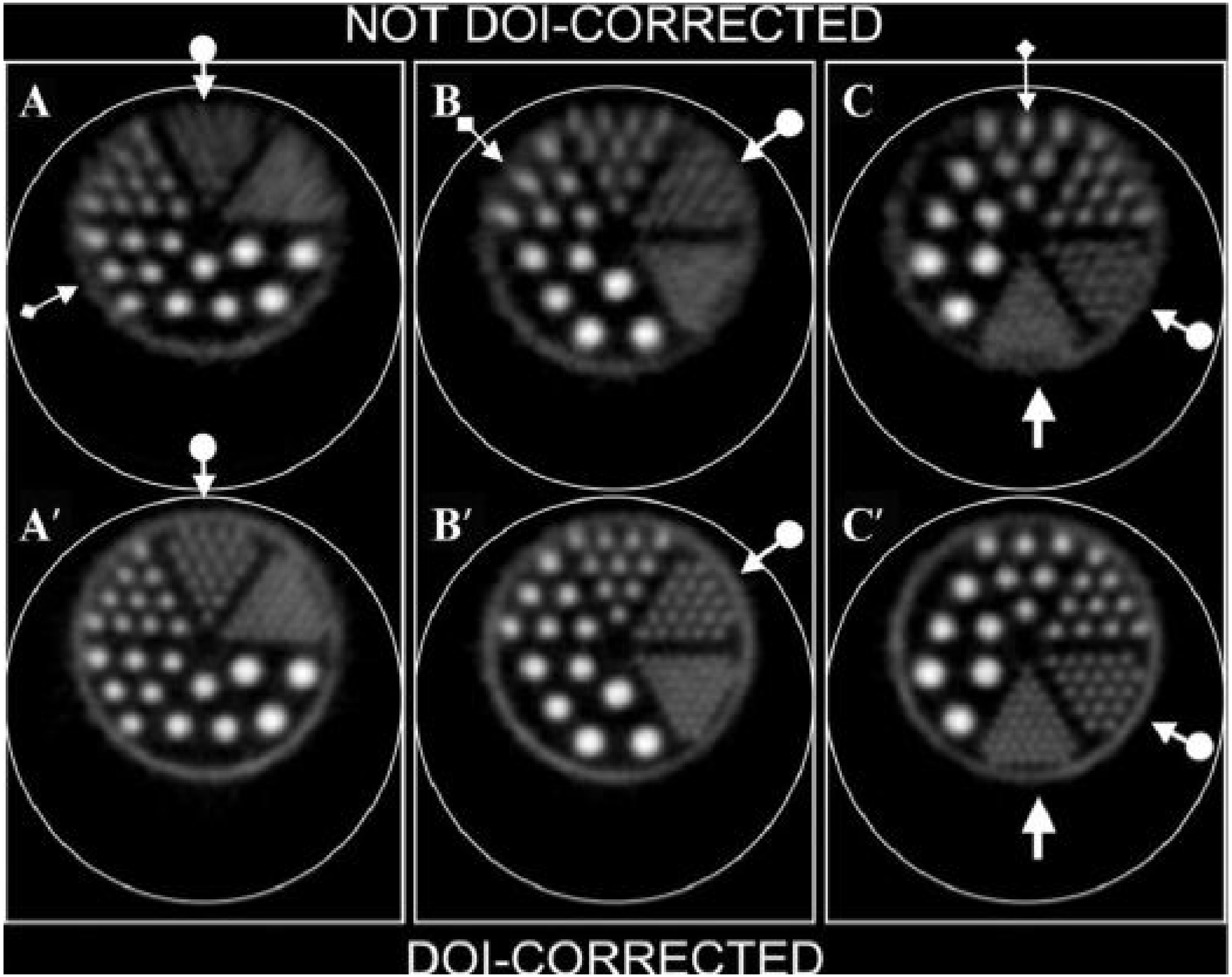


Parallax error degrades the resolution at the edges of the scanner



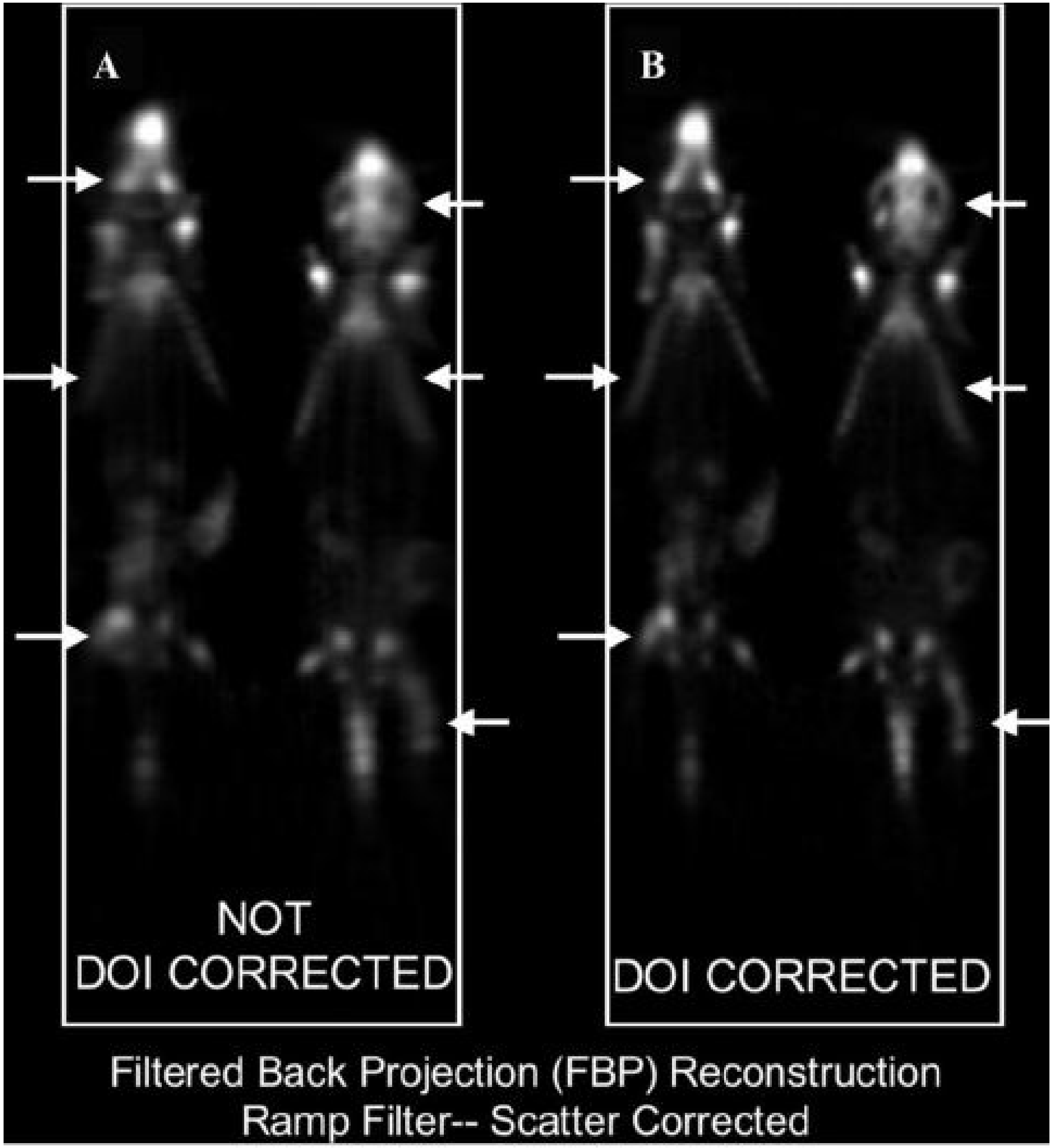


DOI determination



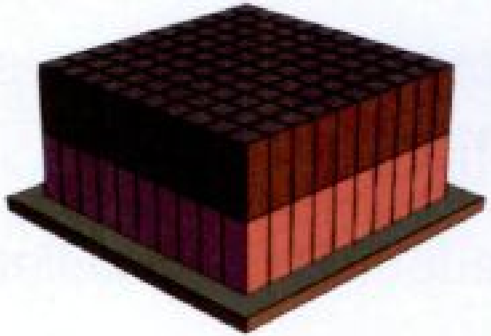
Green et al.Molec. Im. 9(6) 2010

DOI determination

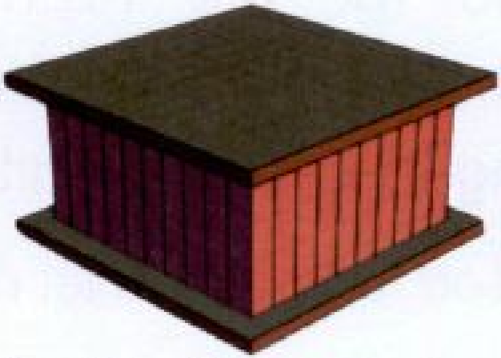


Green et al.Molec. Im. 9(6) 2010

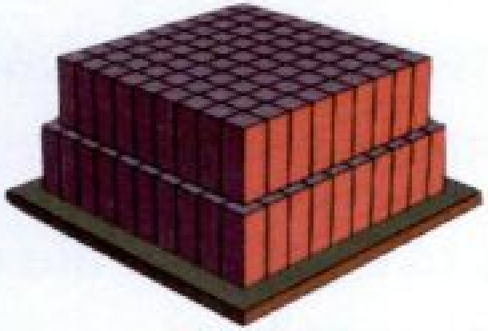
DOI determination



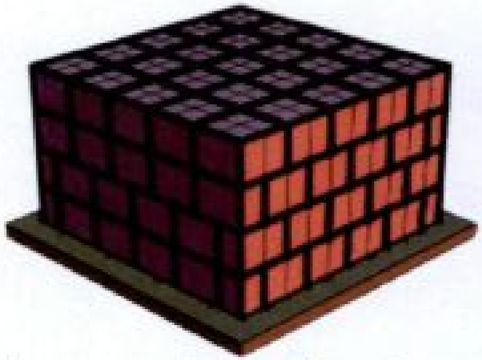
Phoswich design



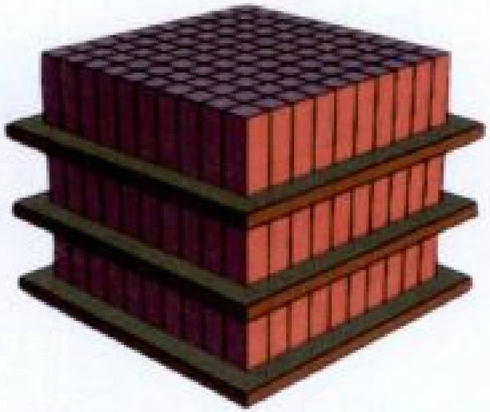
Double-sided readout



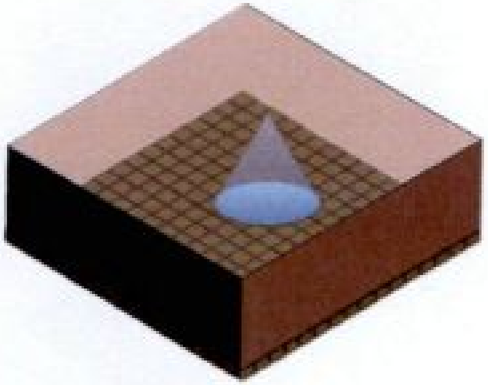
Stacked layers with a relative displacement with respect to each other



Layers with reflective optical structure

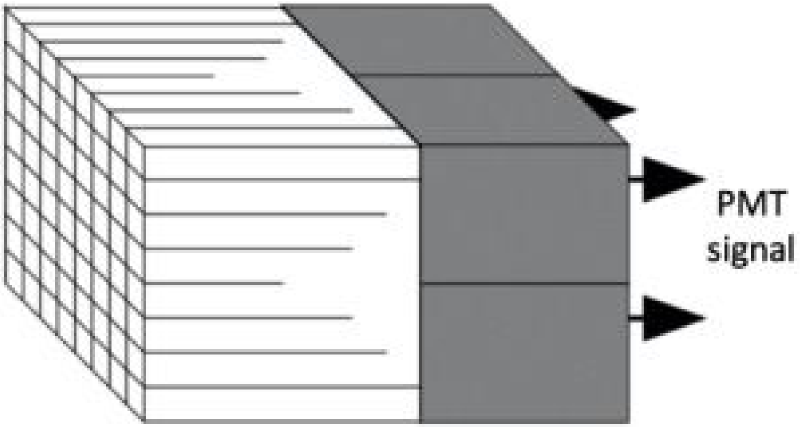


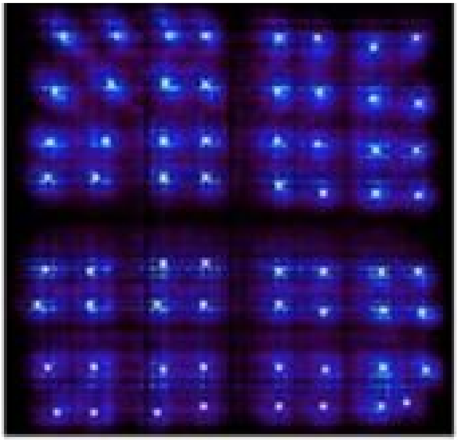
Multiple photosensors

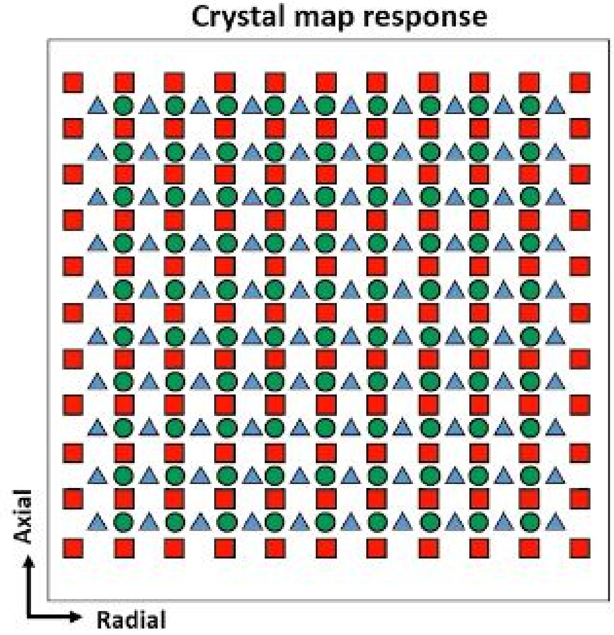


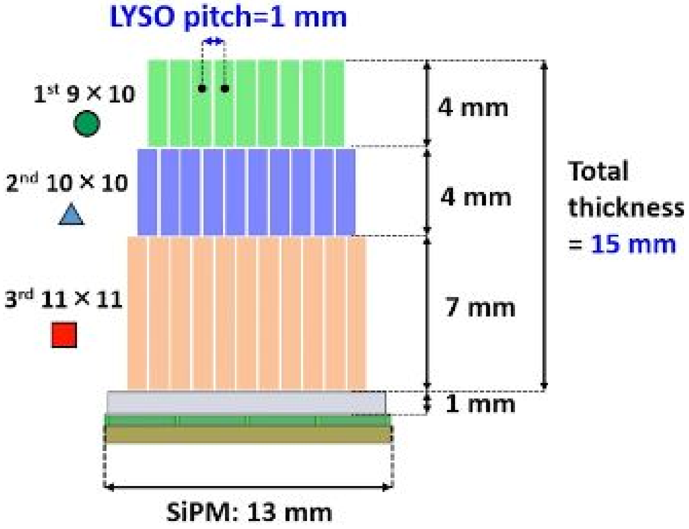
Width of the light spot in continuous scintillators

DOI determination



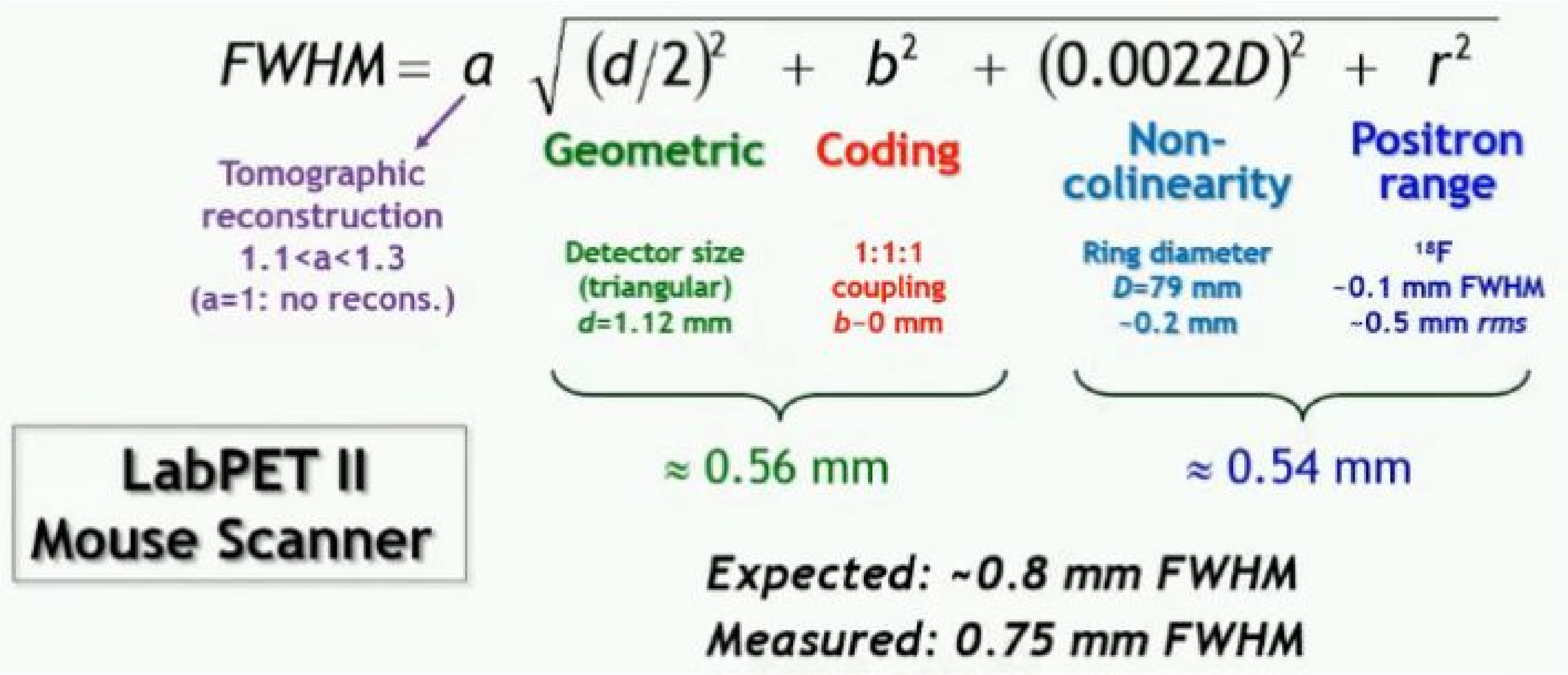






Higher cost
Generally not included in scanners

Spatial resolution



$$FWHM = a\sqrt{(d/2)^2 + b^2 + (0.0022D)^2 + r^2}$$

Tomographic reconstruction
1.1<a<1.3
(a=1: no recons.)

Geometric
Detector size
(triangular)
d=1.12 mm

Coding
1:1:1
coupling
b-0 mm

≈ 0.56 mm

Non-colinearity
Ring diameter
D=79 mm
-0.2 mm

Positron range
^{18}F
-0.1 mm FWHM
~0.5 mm *rms*

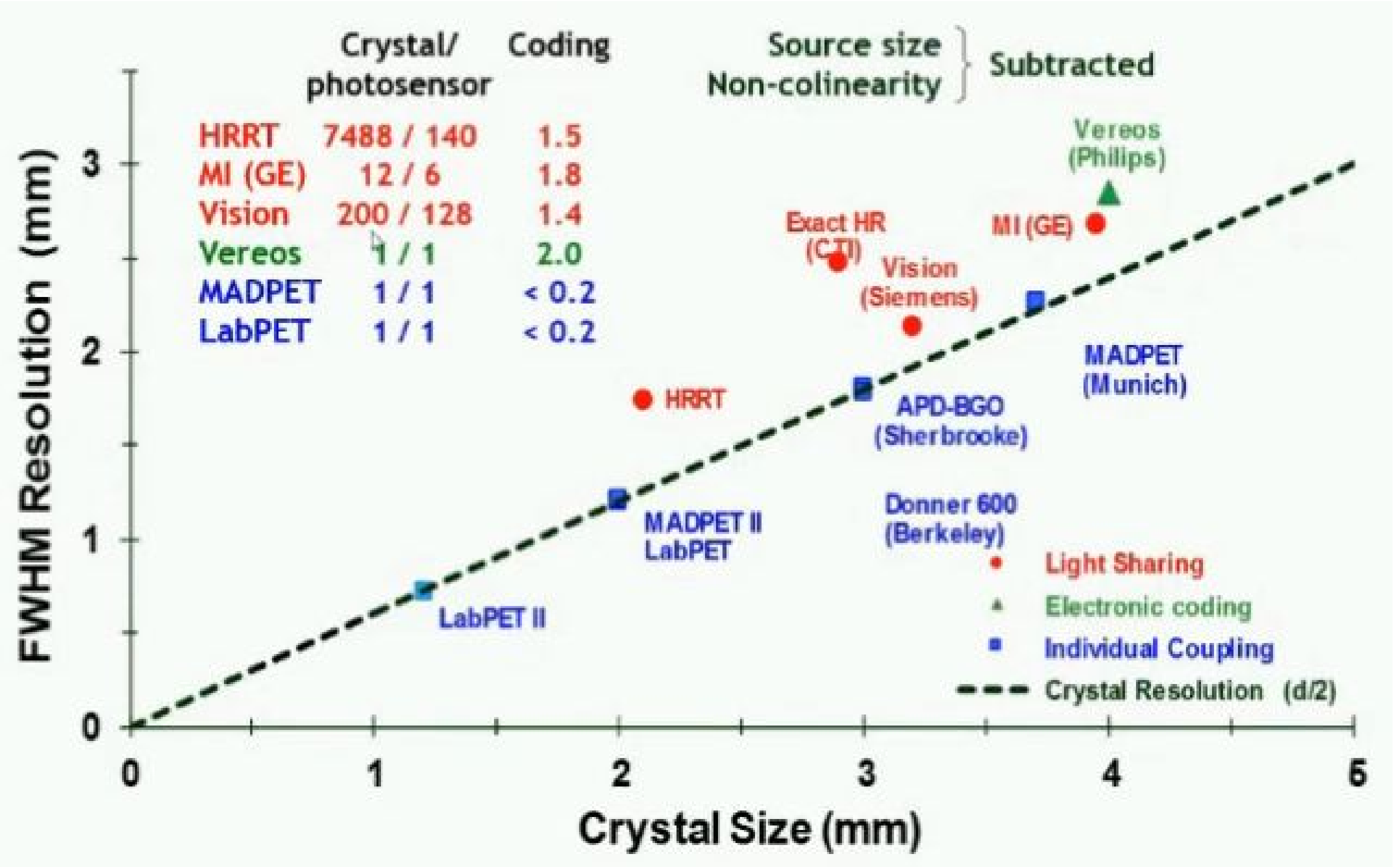
≈ 0.54 mm

LabPET II
Mouse Scanner

Expected: ~0.8 mm FWHM
Measured: 0.75 mm FWHM

Spatial resolution in PET scanners

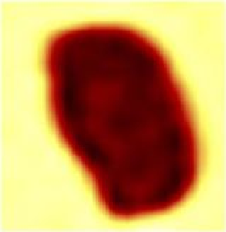
Small animal and dedicated scanners



	Crystal/ photosensor	Coding
HRRT	7488 / 140	1.5
MI (GE)	12 / 6	1.8
Vision	200 / 128	1.4
Vereos	1 / 1	2.0
MADPET	1 / 1	< 0.2
LabPET	1 / 1	< 0.2

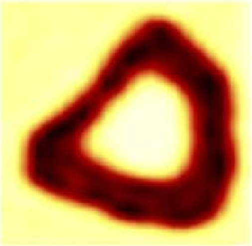
Source size
Non-colinearity } Subtracted

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



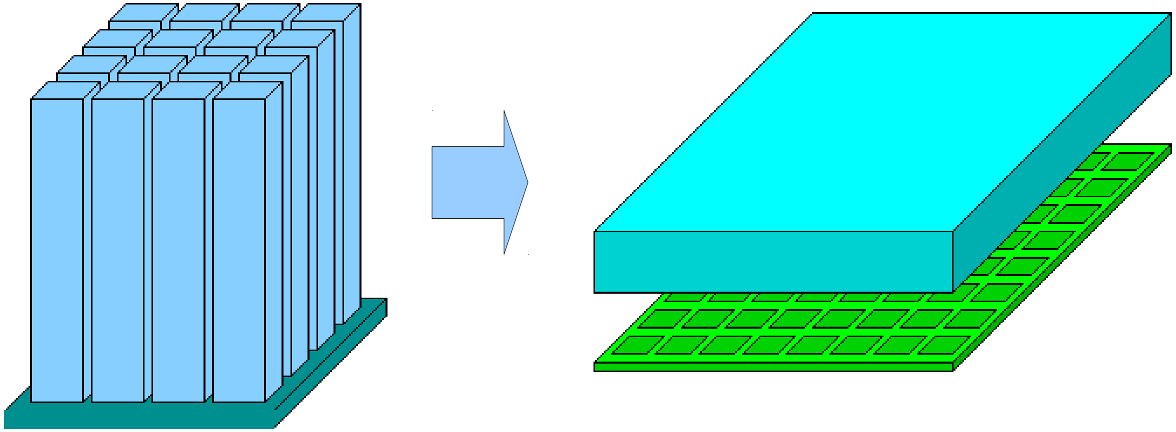
Tumor 1

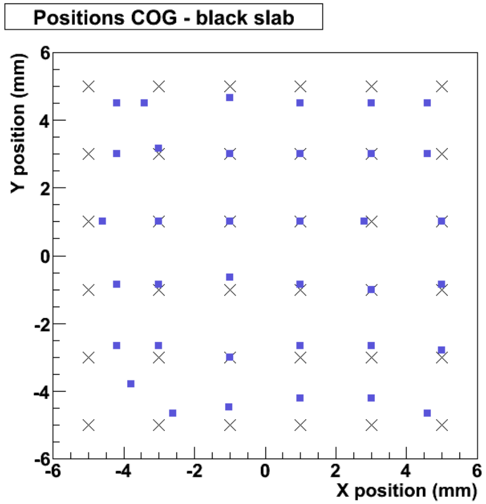
Tumor 2



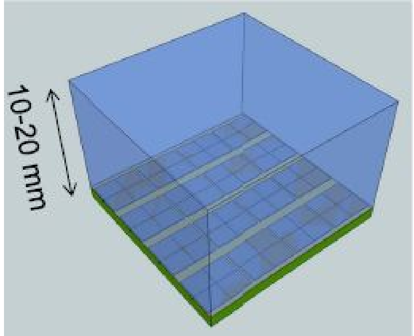
Tumor 3

Monolithic detectors?





Neural Networks trained with Monte -Carlo simulations are promising



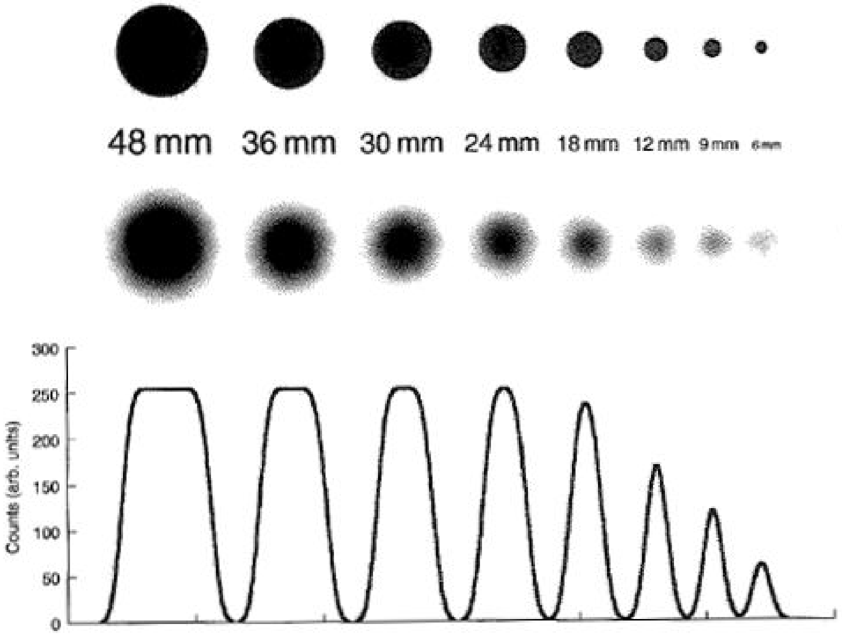
D. Schaart.
ICTR-PHE 2014

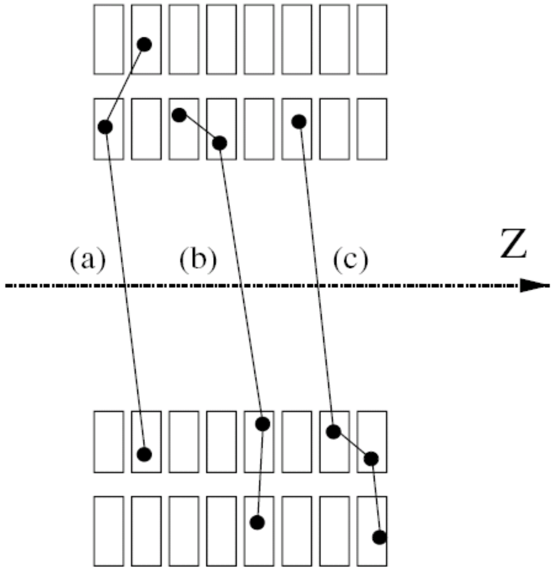
Performance parameter		Monolithic	State of the art
Energy resolution	(% FWHM)	11 - 12	~12
Spatial resolution	(mm FWHM)	1.0 - 1.6	4 - 6
DOI resolution	(mm FWHM)	3 - 5 mm	None
CRT	(ps FWHM)	160 - 185	500 - 650

Image reconstruction and degradation compensation

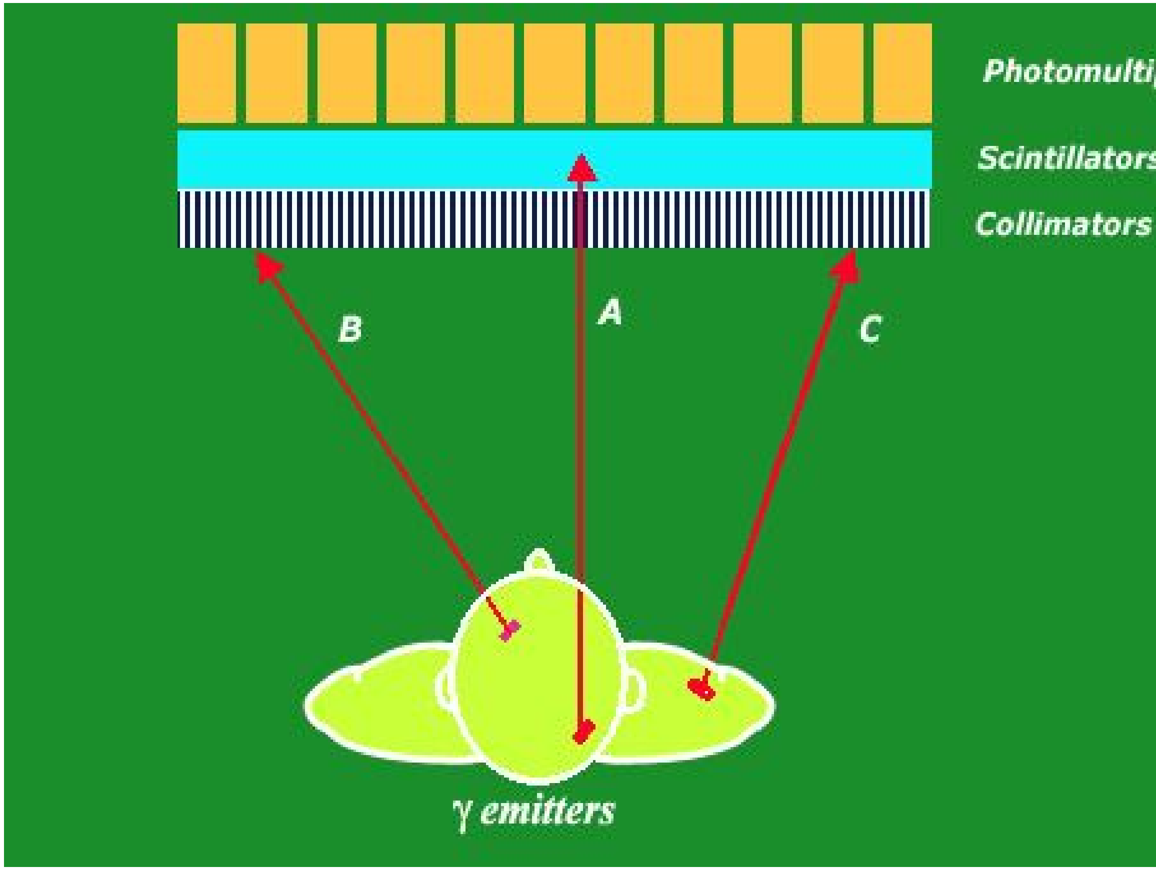
- Faster algorithms
- More accurate images – better modelling of underlying physics
- TB-PET – all angles.

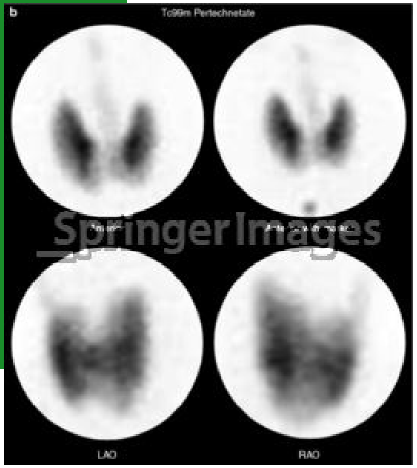
- Attenuation
- Scattering in patient
- Parcial volume effects
- Random coincidences estimation
- Scattering in the detector
- Patient/organ movements



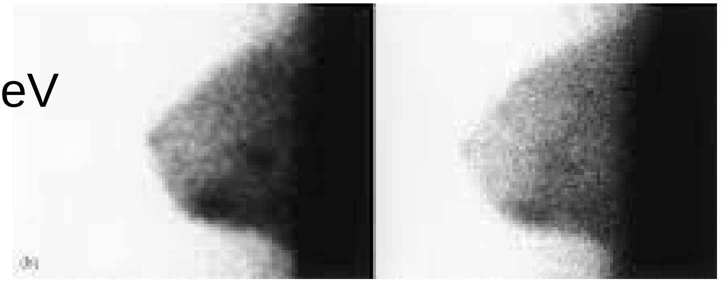


Gamma cameras



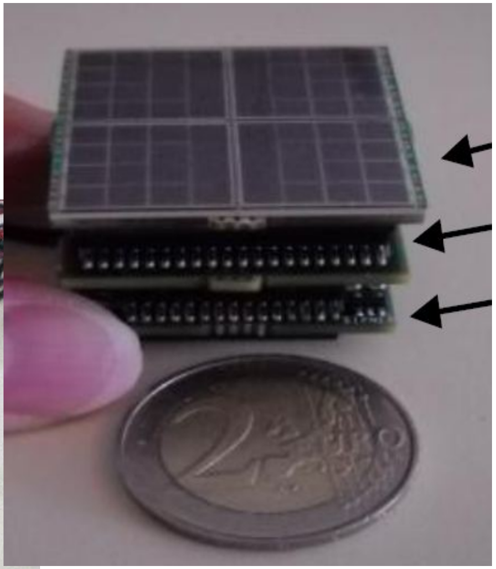


- Single photon emitters
- Most common radiotracer: ^{99m}Tc- 140 keV



Gamma cameras

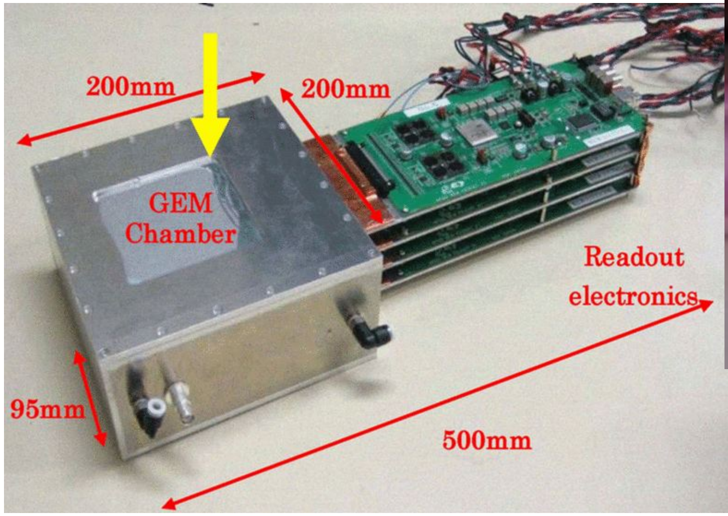
Small, dedicated systems (heart, breast…): mostly scintillators, but other types considered.

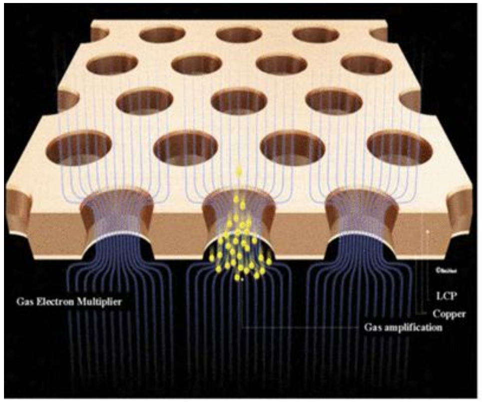


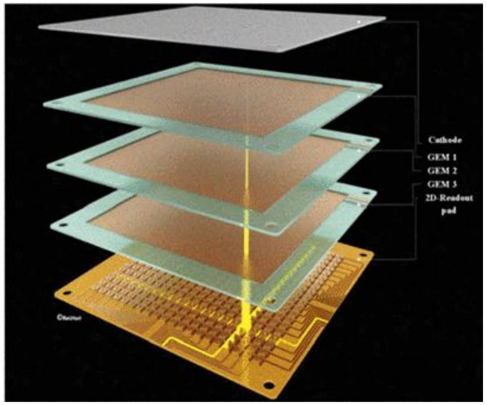
SiPM board

ASIC board

FPGA board



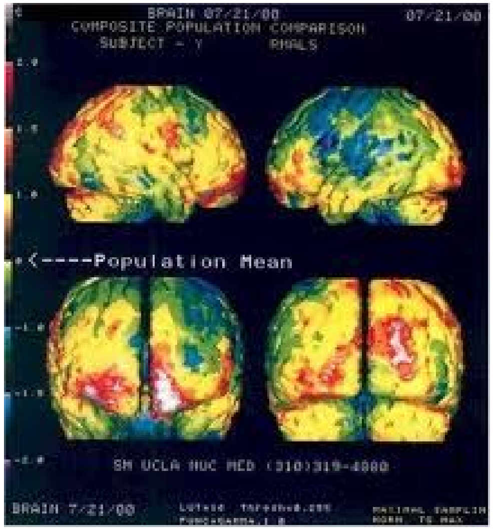


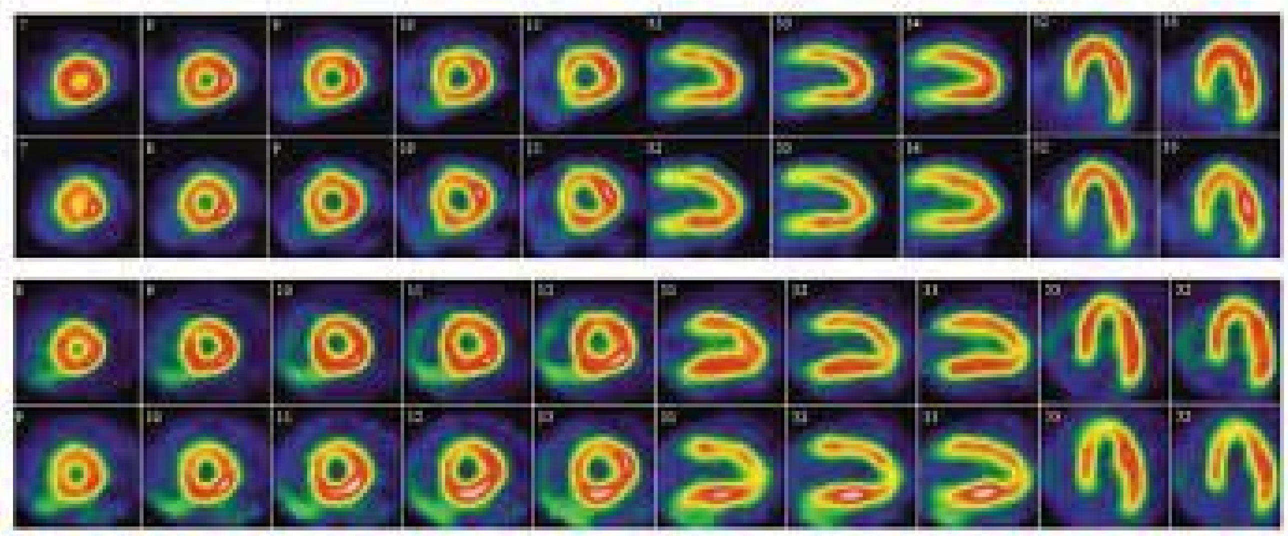


CZT, I. Blevis et al. 2011 IEEE NSS MIC conf record.
LaBr3, R. Pani et al 2015 JINST 10 C06002.
GEM- T. Koike et al. 2011 IEEE NSS MIC conf record.

Single Photon Emission Computed Tomography (SPECT)

NM/CT 860 | GE HealthCare

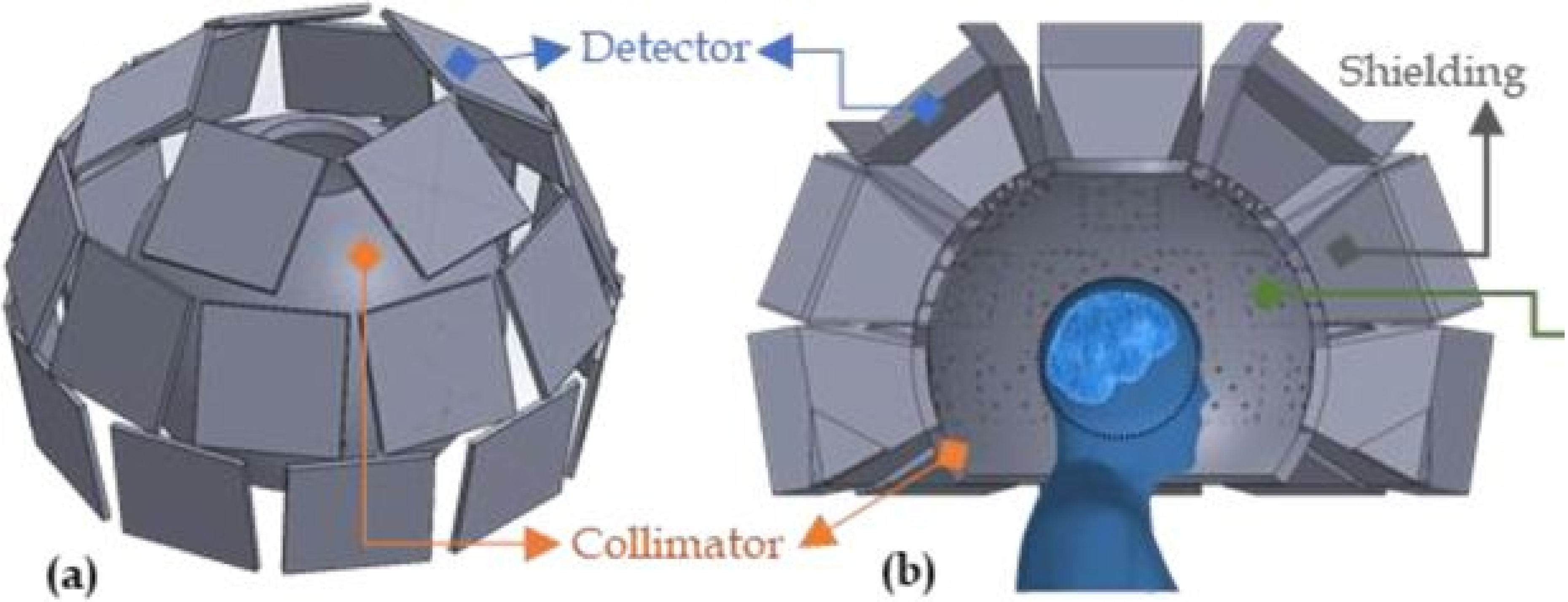




SPECT

Dedicated systems

Mutipinhole brain SPECT

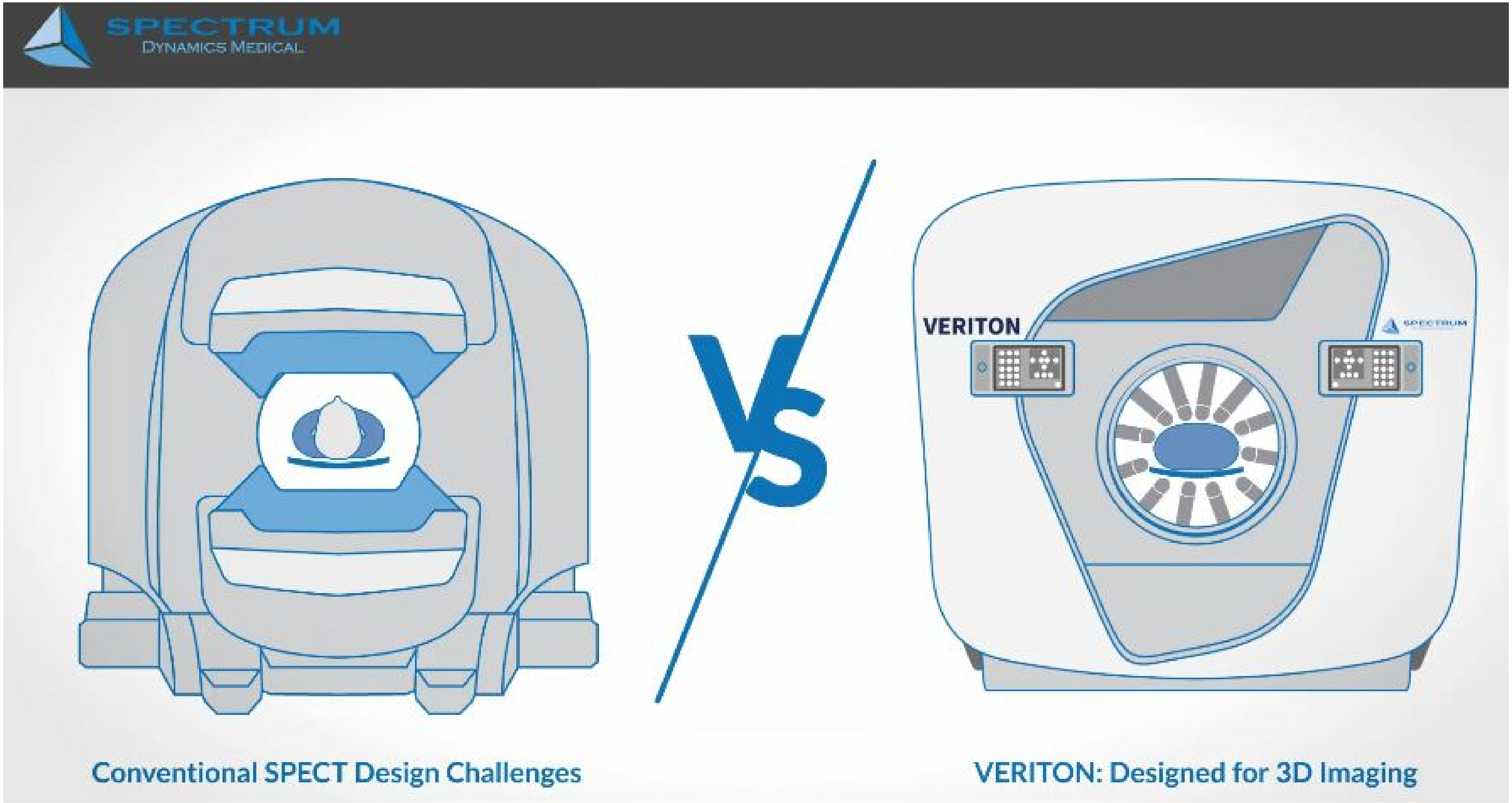


N. Zeraatkar et al. Biomed Phys Eng Express. 2021

SPECT

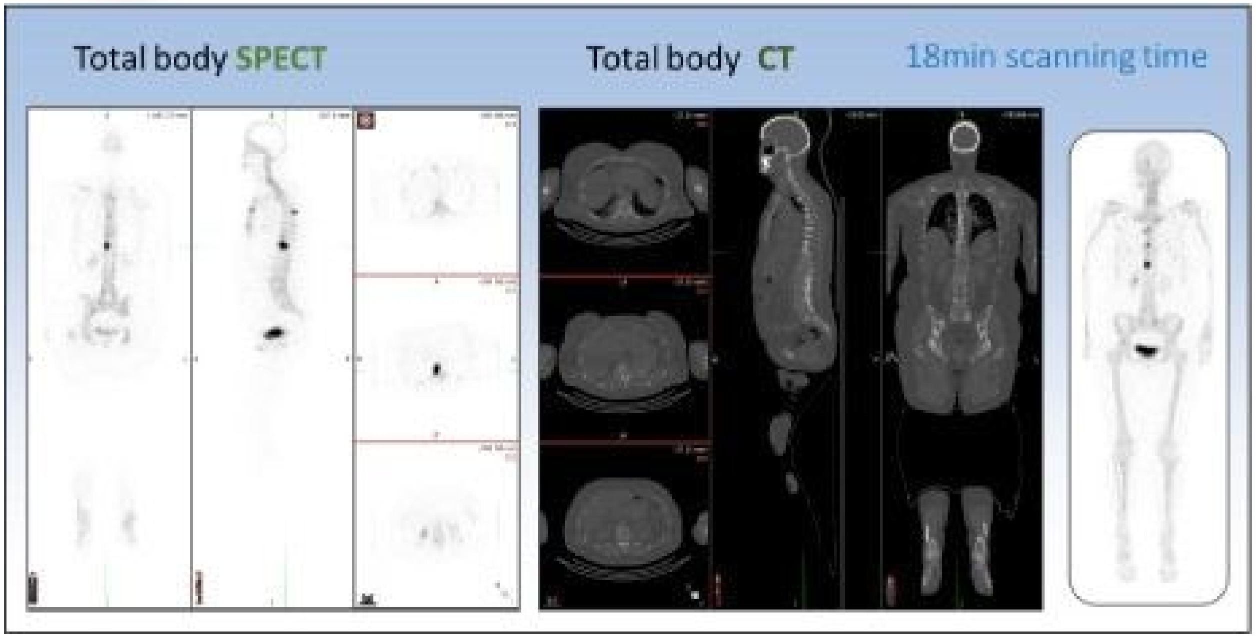
Veriton-CT (Spectrum Dynamics Medical)

CZT detectors. Only SPECT, no gamma camera.

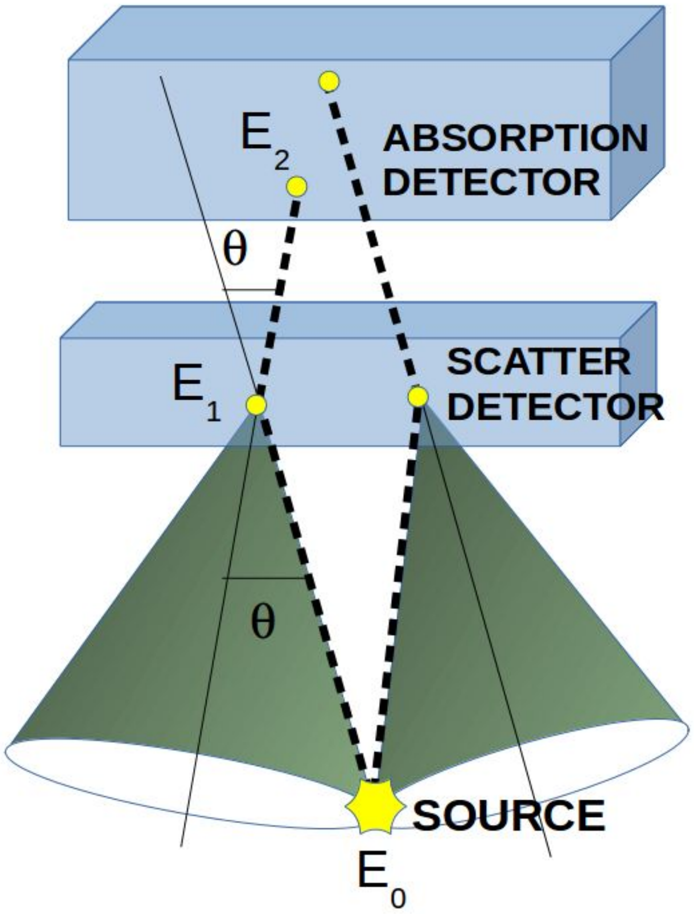


SPECT

Veriton-CT (Spectrum Dynamics Medical)



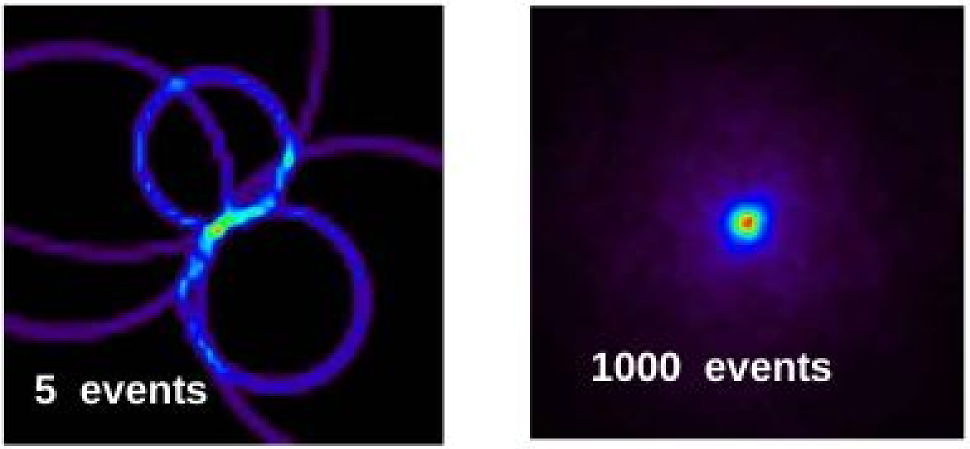
Compton cameras



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

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

Backprojection

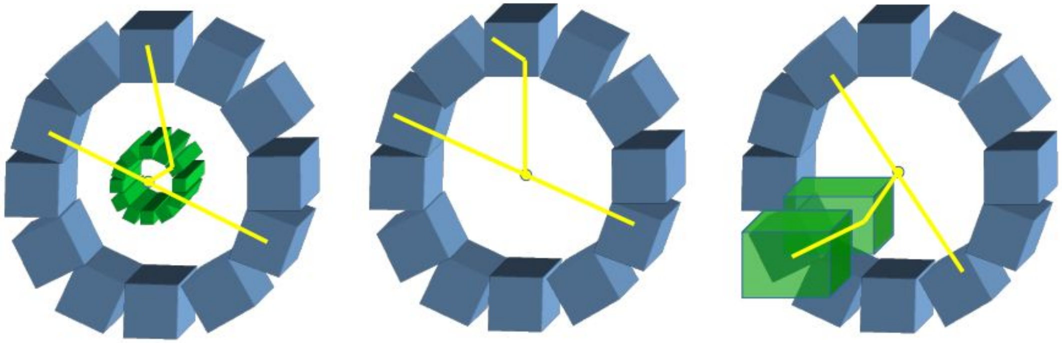


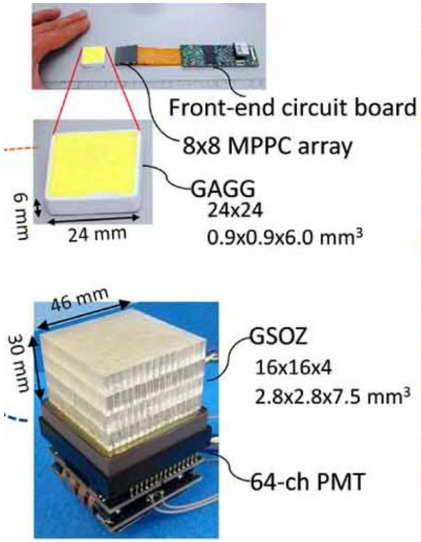
+ Image reconstruction

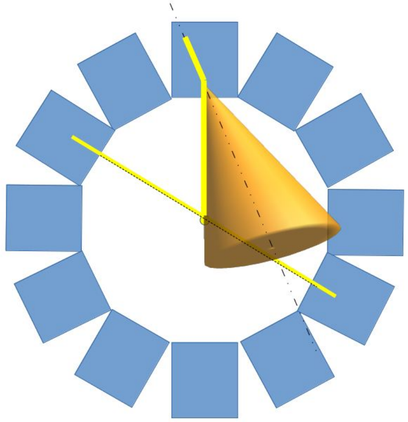
- Higher efficiency than gamma cameras
- Better at higher energies
- Better for multiple energies

Compton-PET / WGI

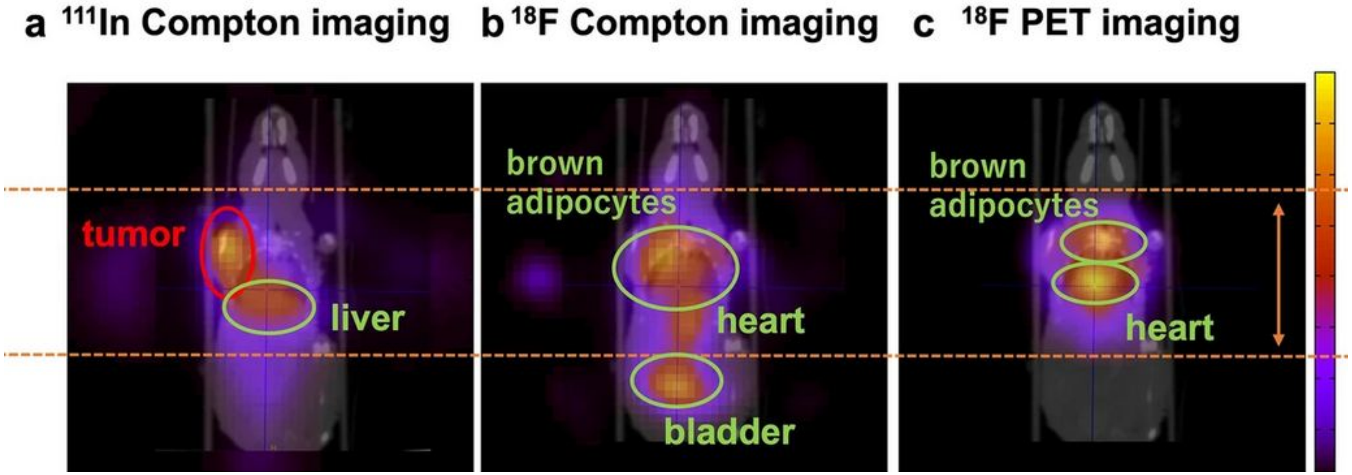
PET and gamma tracers simultaneously



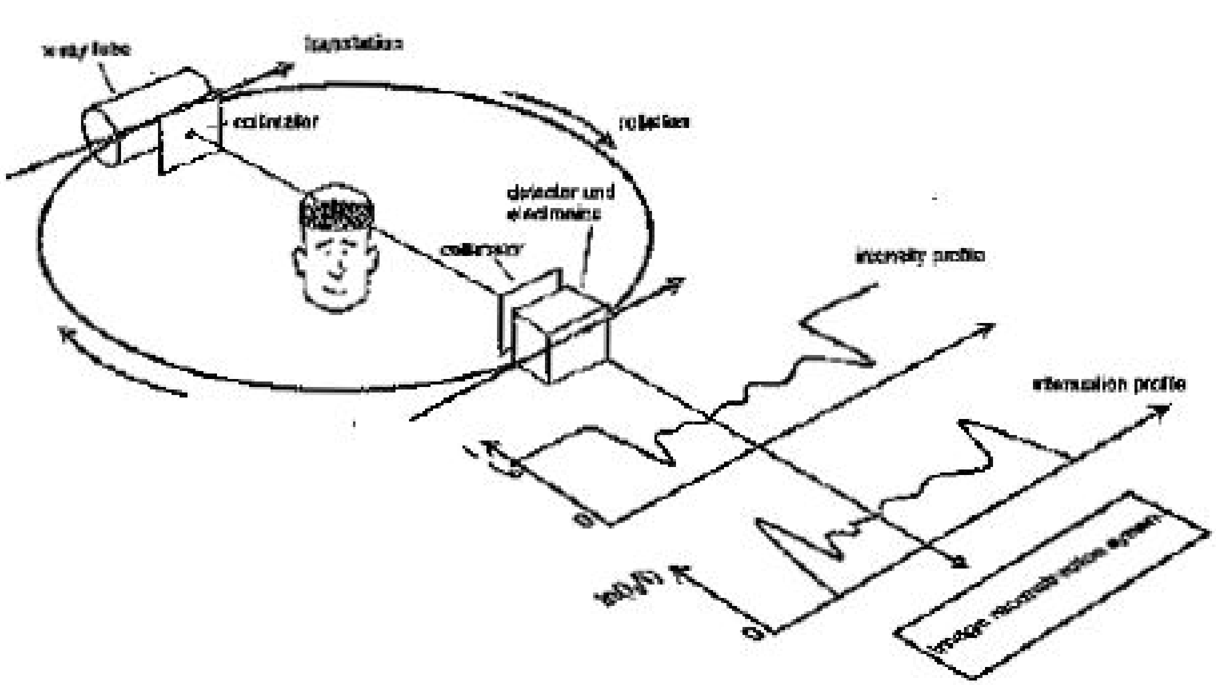


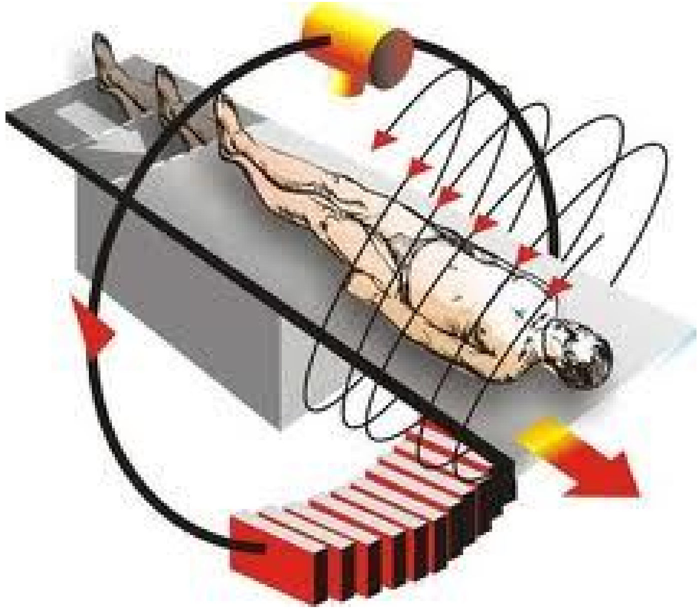


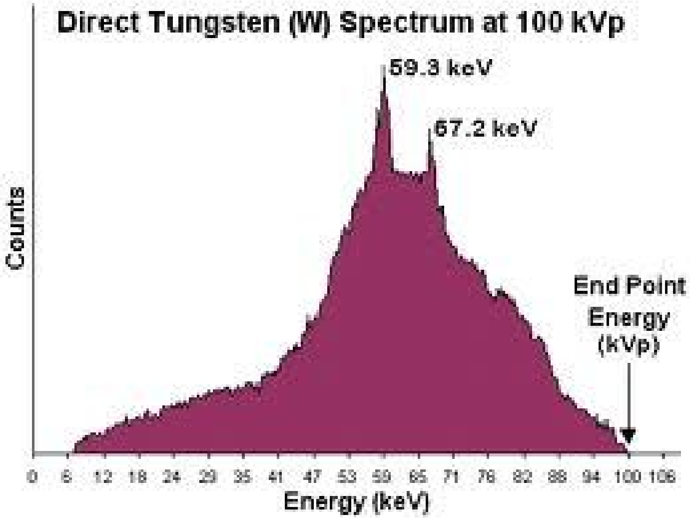
Three gamma imaging
^{89}Zn



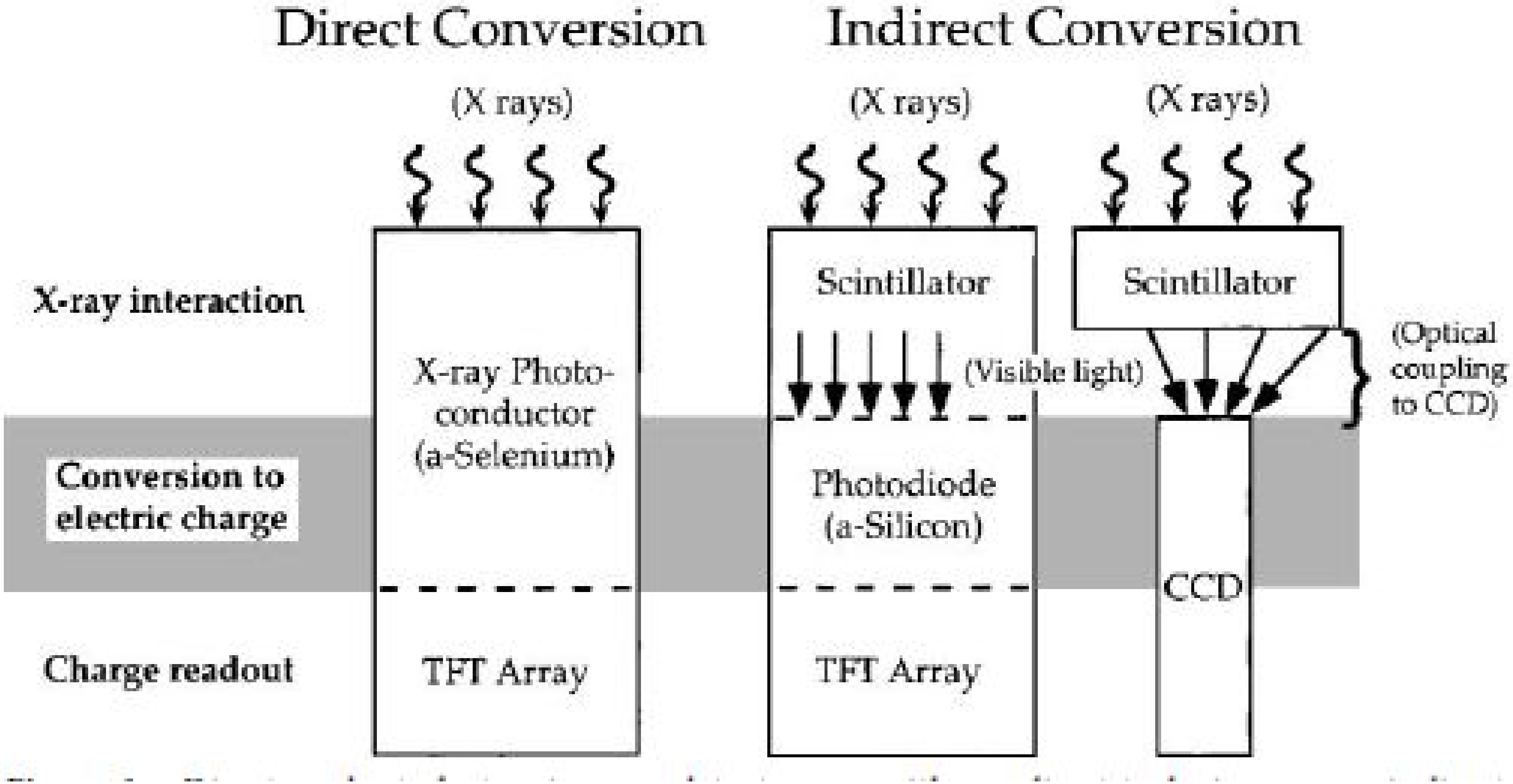
X-rays and Computed Tomography (CT)





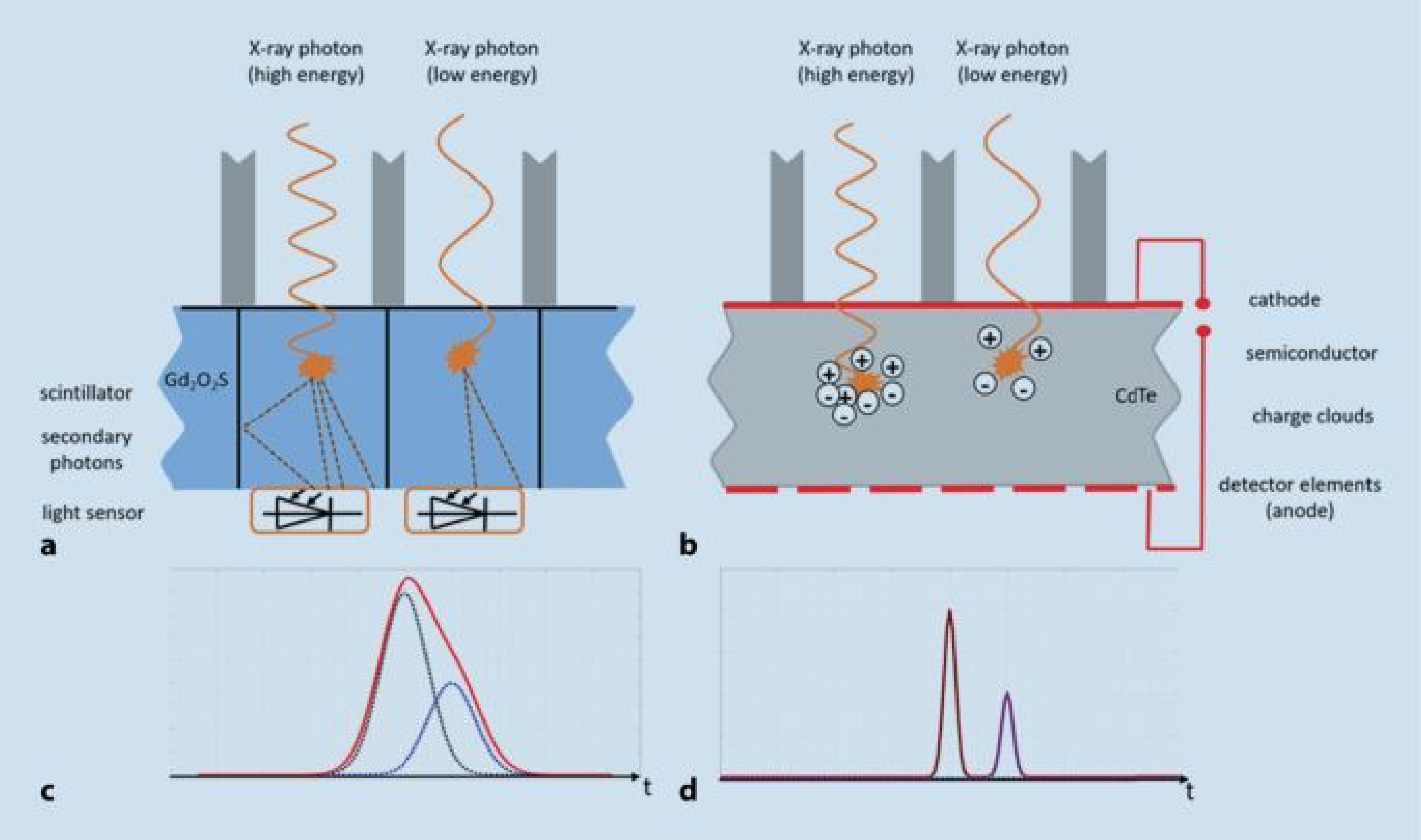


CT detectors




SEM image of CsI crystals

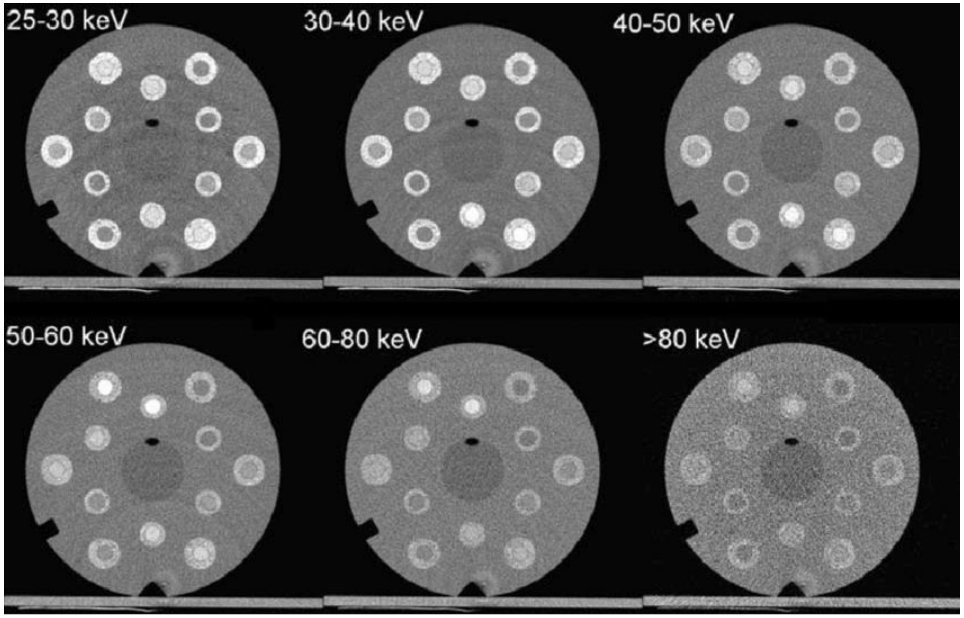
Photon counting CT

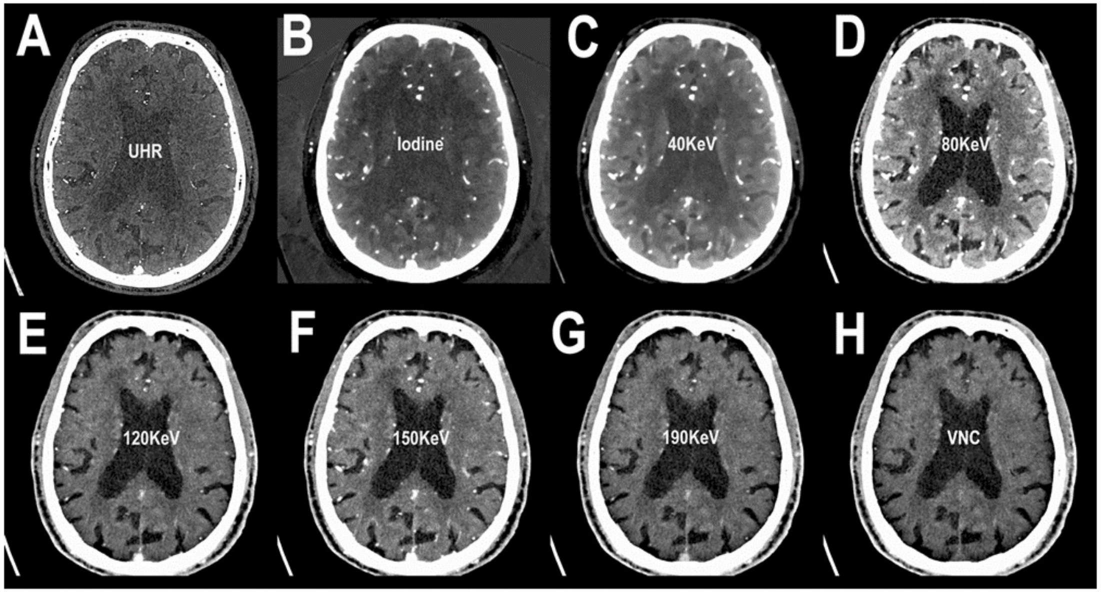


Quantify the energy of each individual photon

→ Images at different energies and reduced noise

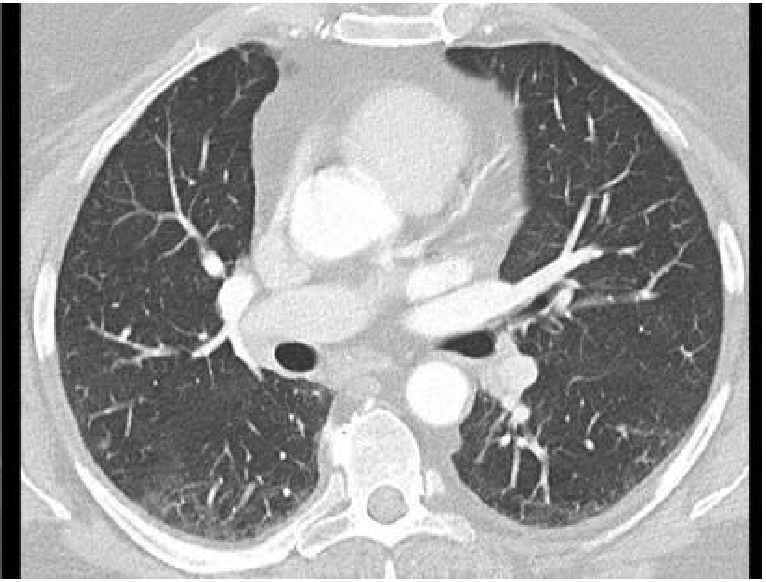
Photon counting CT





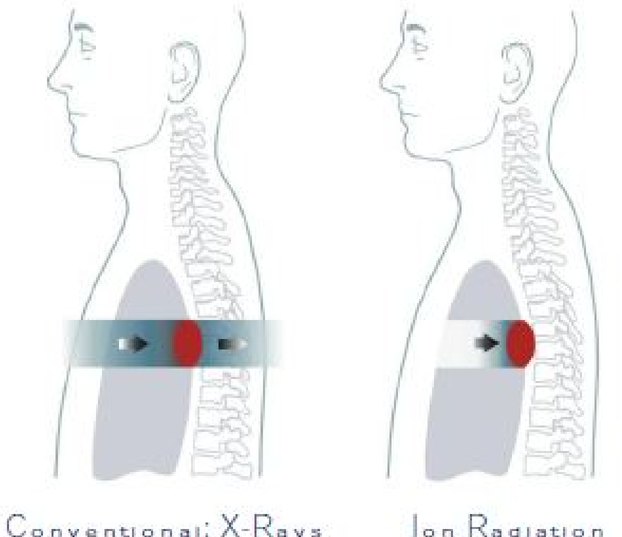
Conventional CT

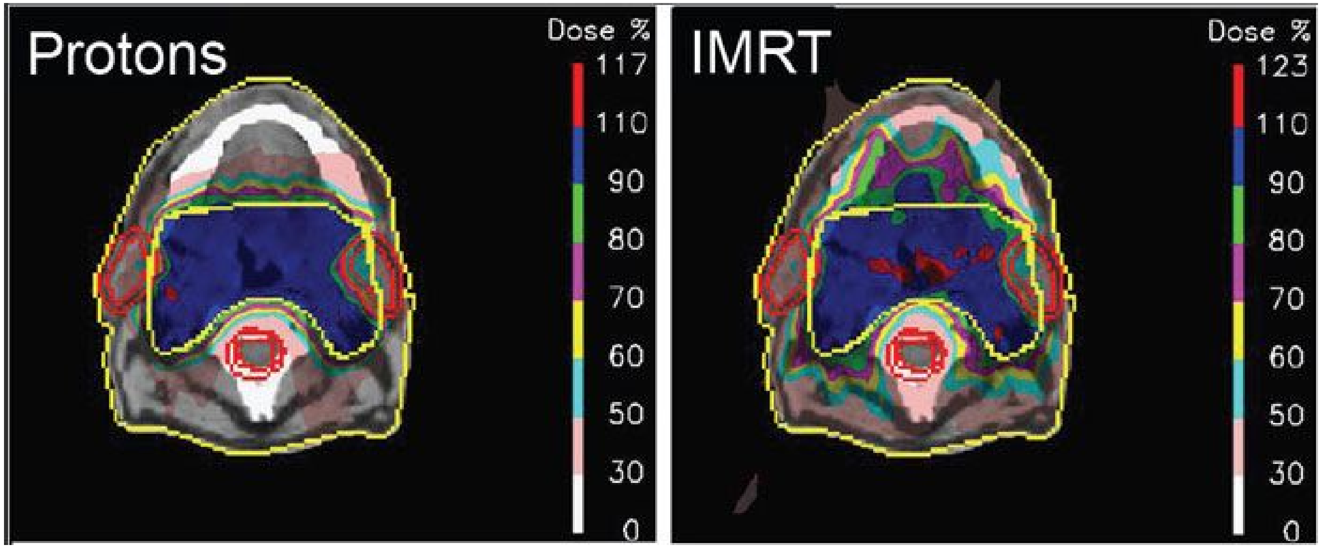
Photon counting CT

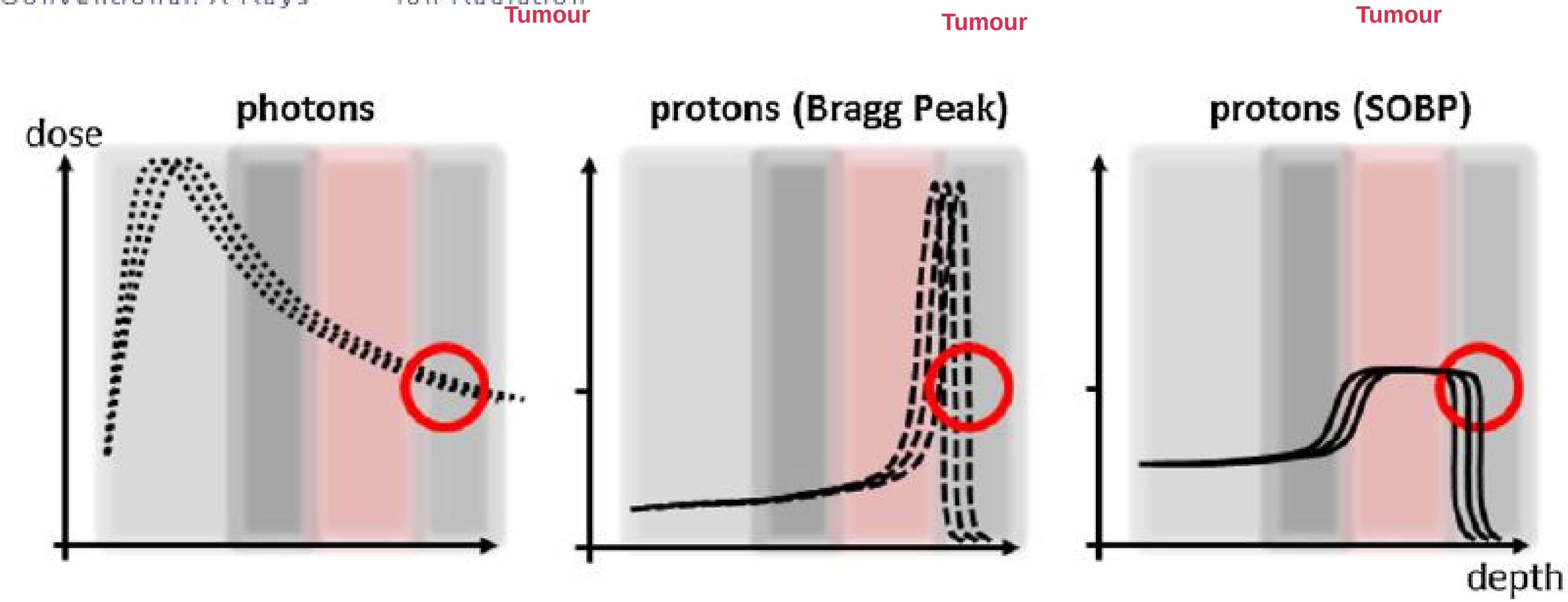


Possible with scintillators? $LaBr_3$?

Hadron therapy treatment monitoring

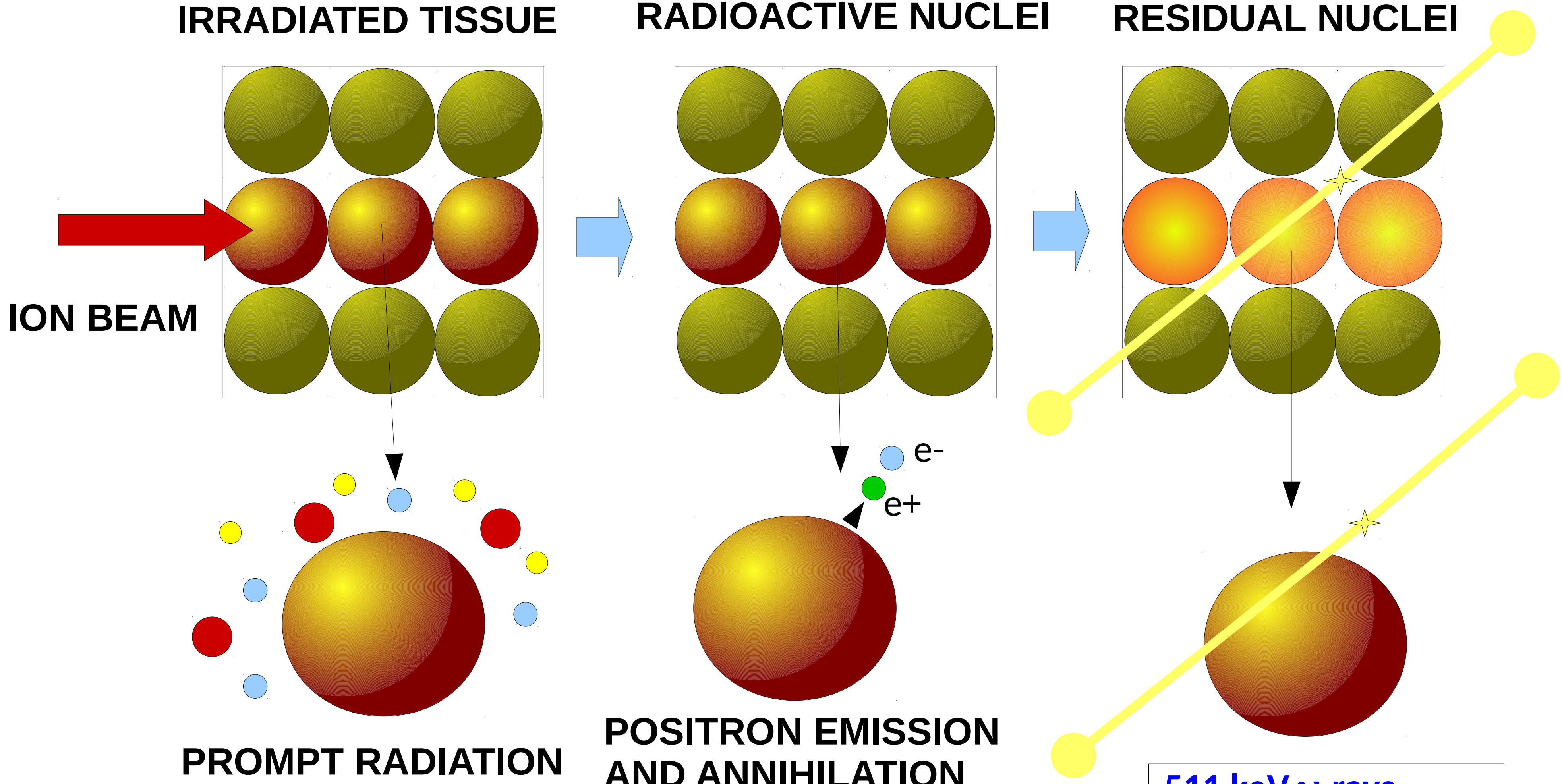






Large safety margins applied to treatment plans.

Hadron therapy treatment monitoring

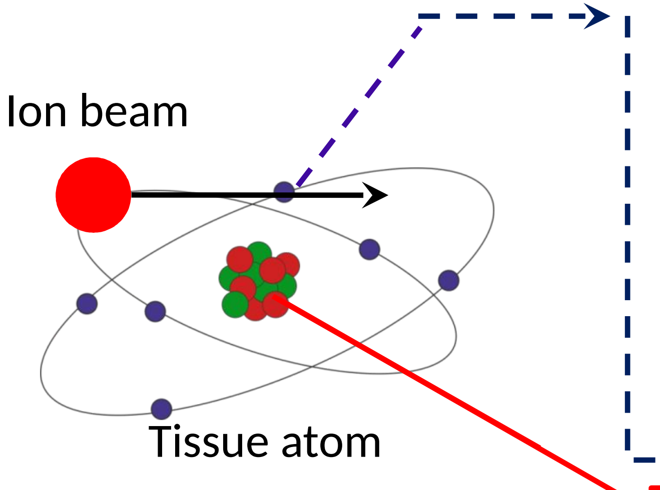


Prompt γ-rays
***E* ~ 1-15 MeV**

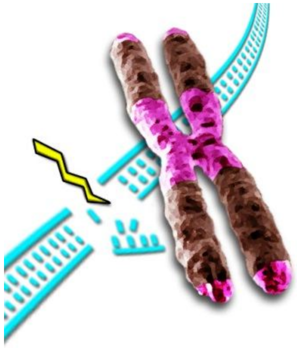
511 keV γ-rays

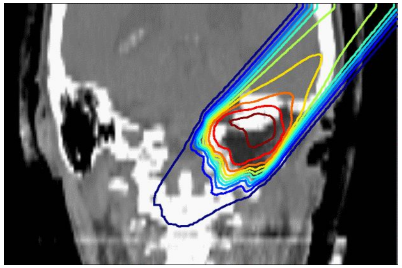
Treatment monitoring

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

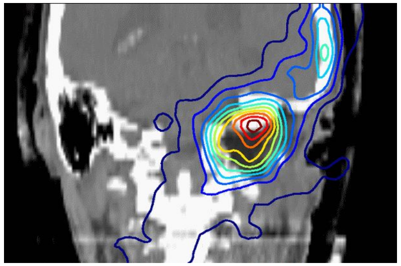


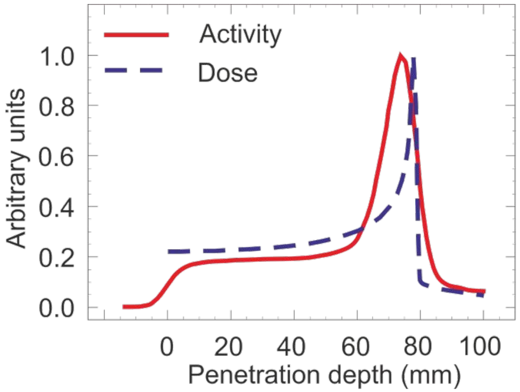
Electromagnetic interaction → Dose deposition



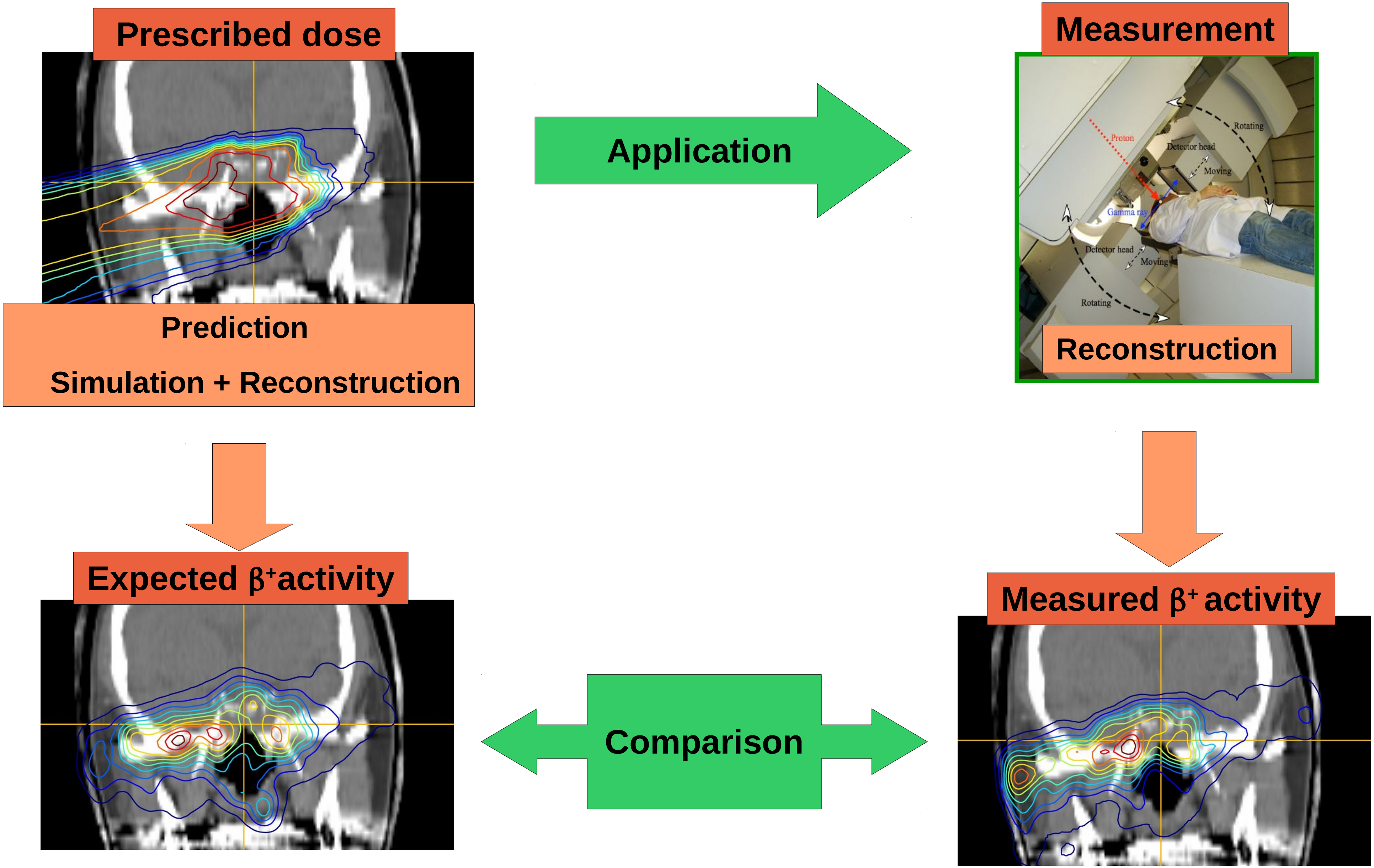


Nuclear Interaction → Secondary particles





Monitoring with PET



Prescribed dose

Application

Measurement

Reconstruction

Prediction

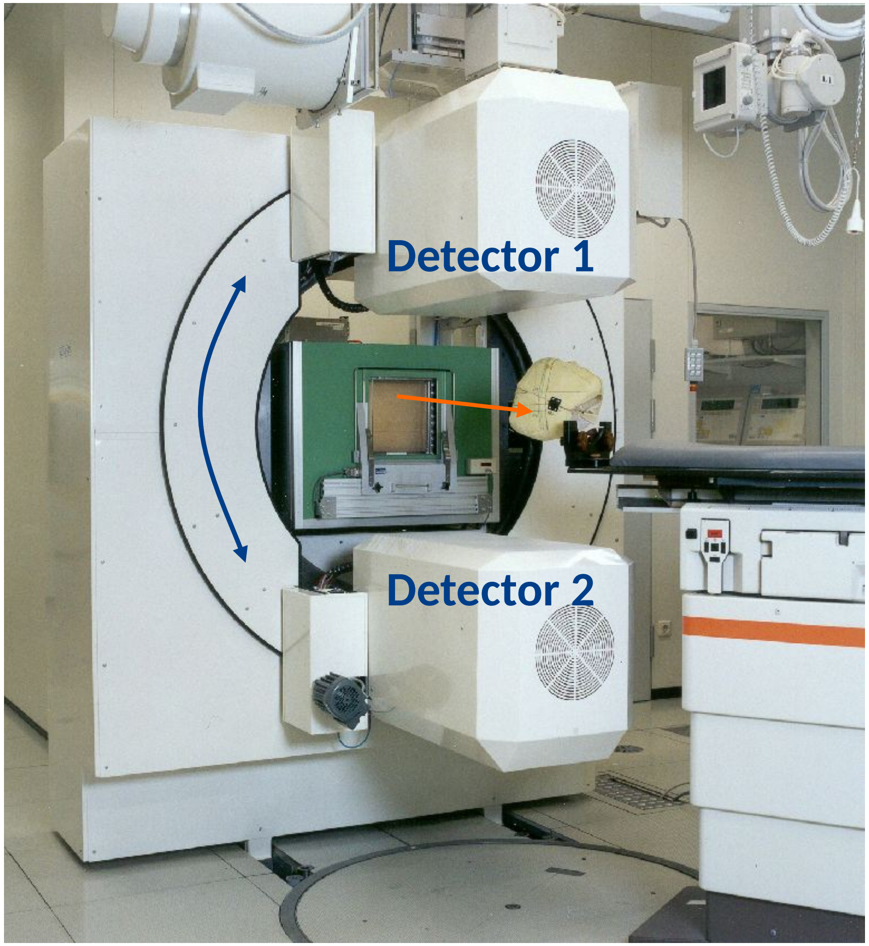
Simulation + Reconstruction

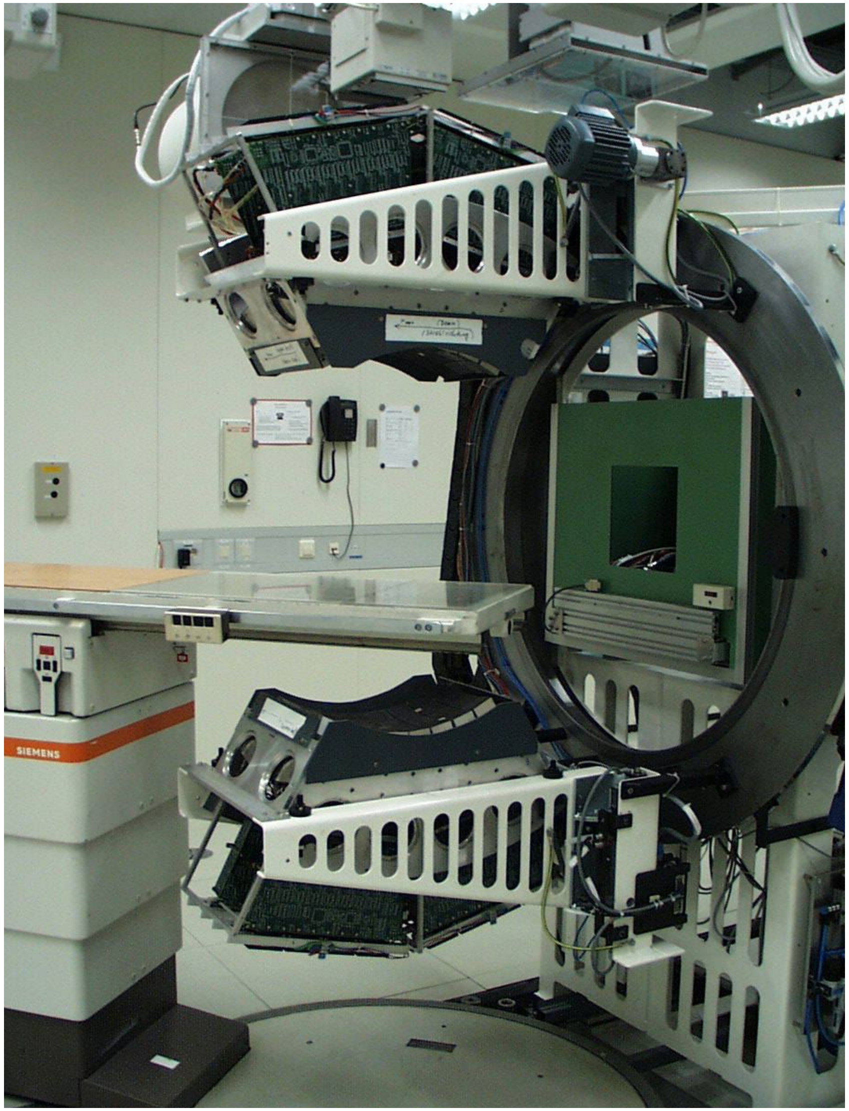
Expected β^+activity

Comparison

Measured β^+ activity

Monitoring with PET

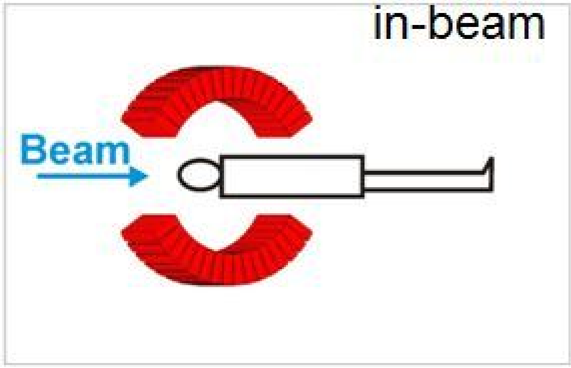


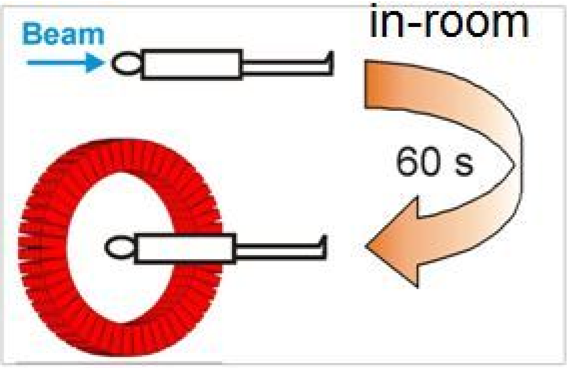


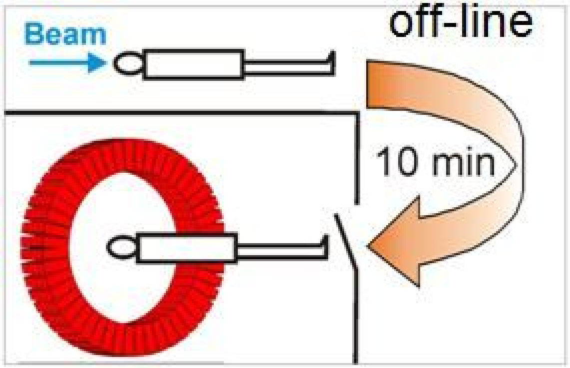
PT PET Scanner @ GSI

Modalities

→ Higher influence of the metabolism, lower beta activity →



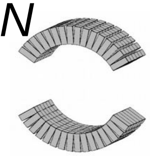
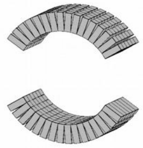


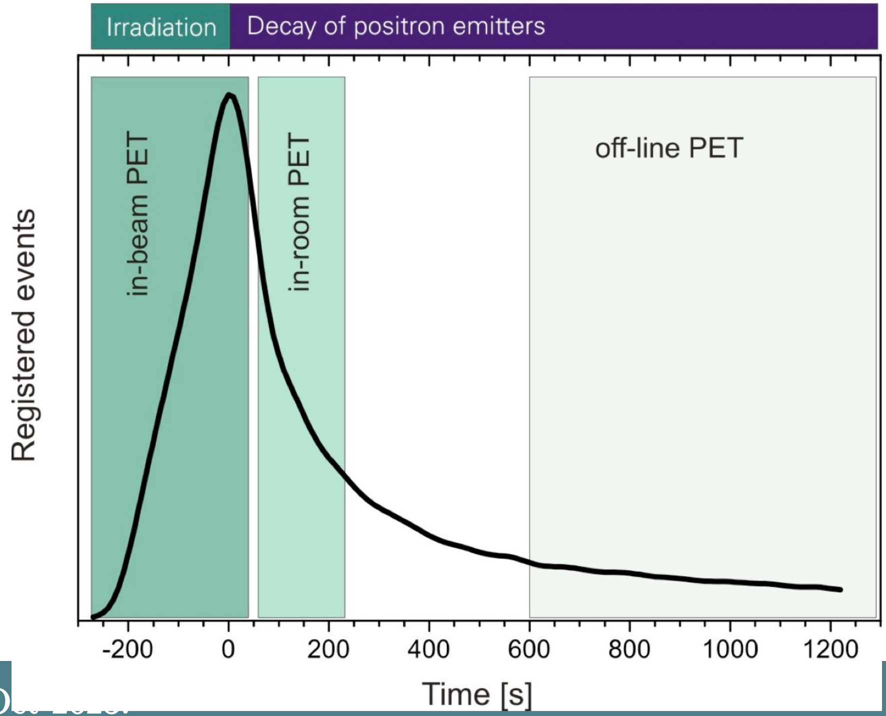


Measurement during irradiation

Measurement shortly after the irradiation

Measurement some time after irradiation

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

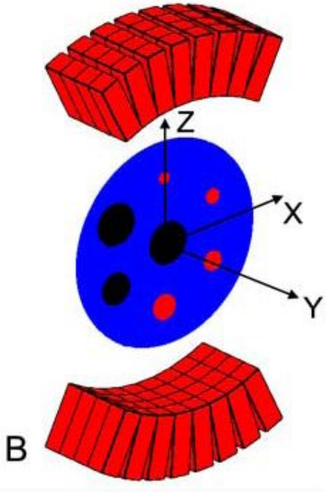


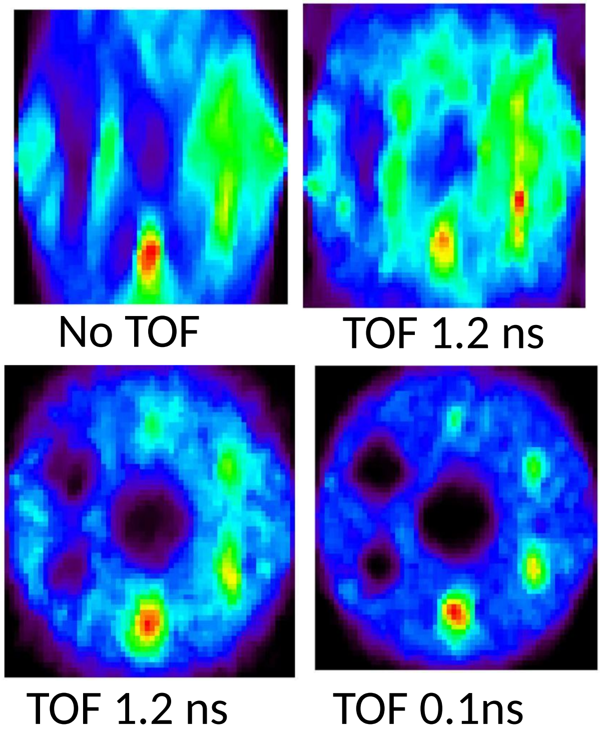
PET Limitations

- 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.

Research

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



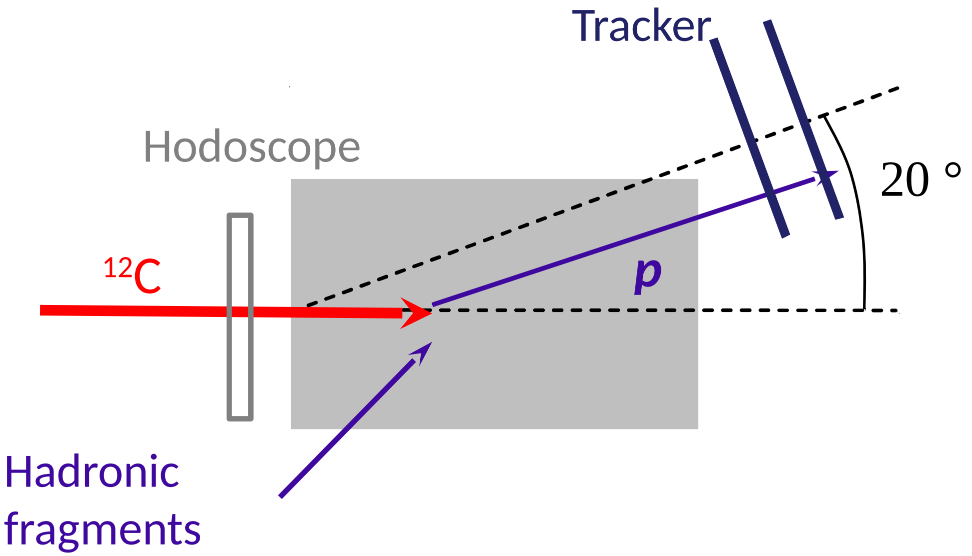


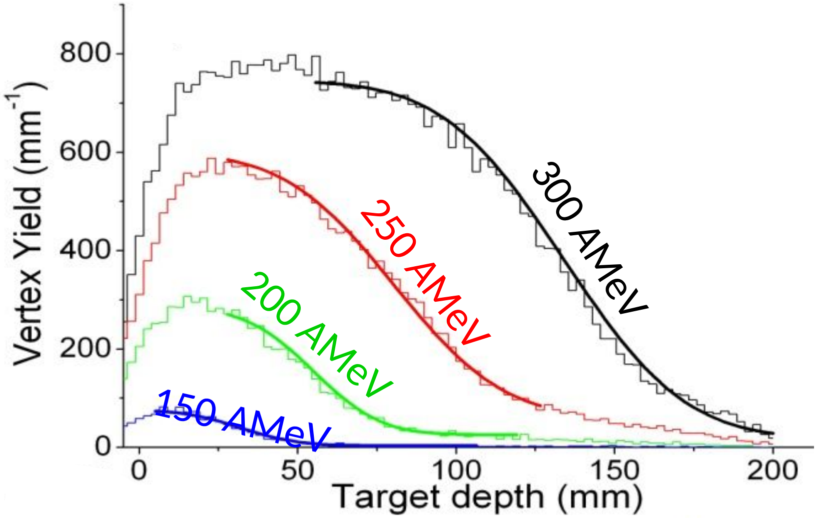
P. Crespo et al.,

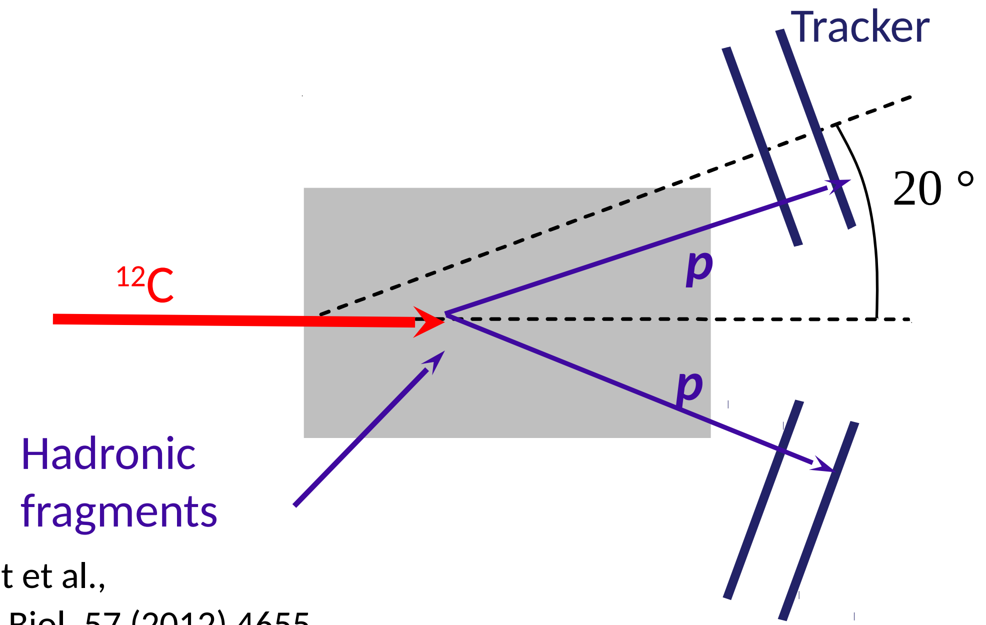
Phys. Med. Biol. 51

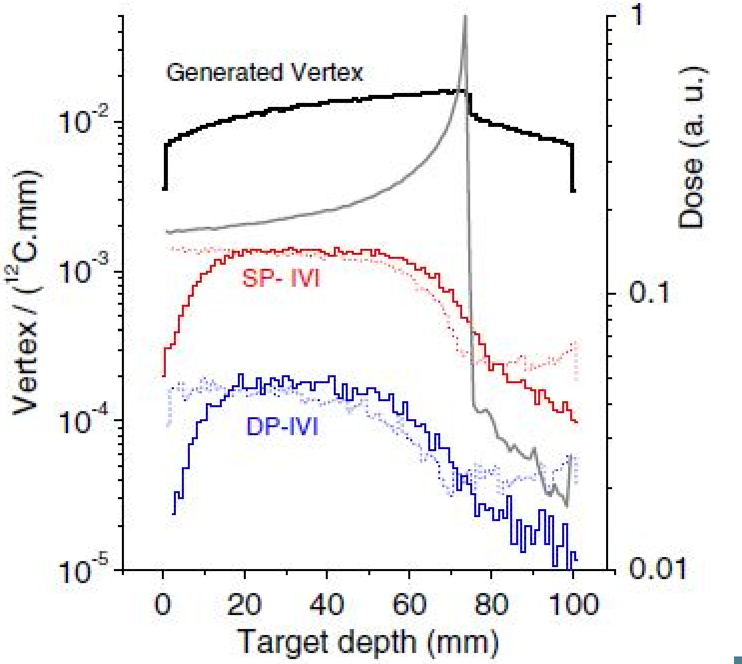
Monitoring with secondary charged particles

Interaction Vertex Imaging (mainly Carbon ions)





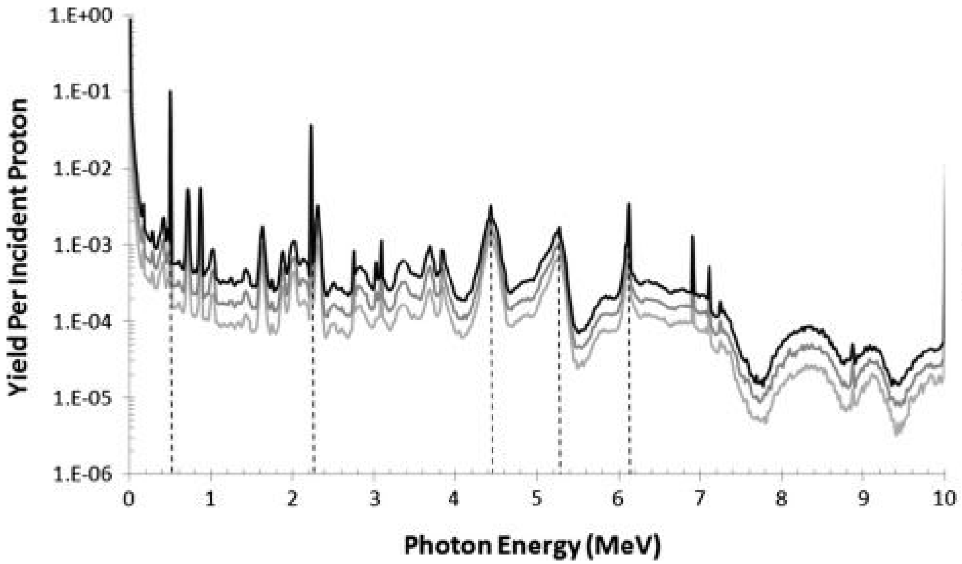


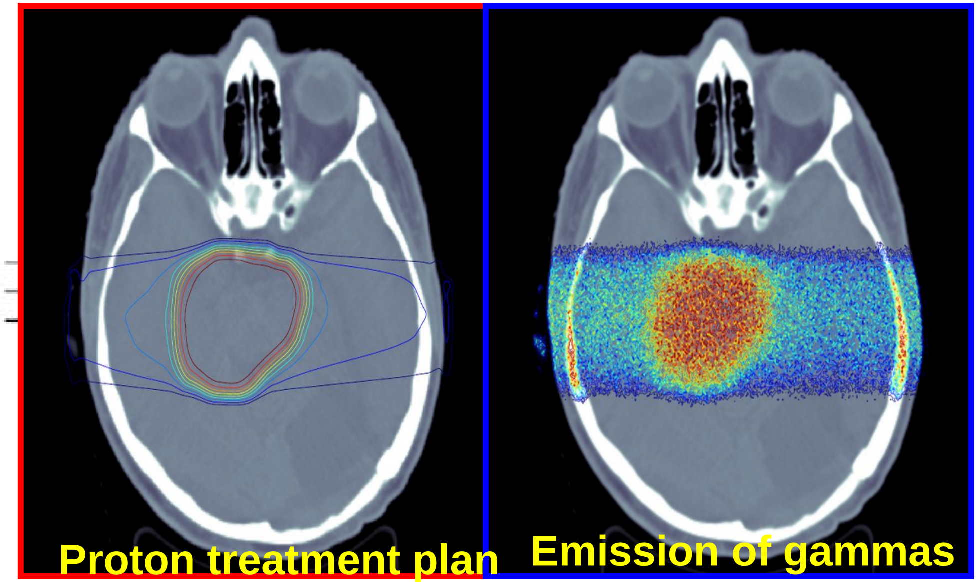


P Henriquet et al.,
Phys. Med. Biol. 57 (2012) 4655

Monitoring with prompt gammas

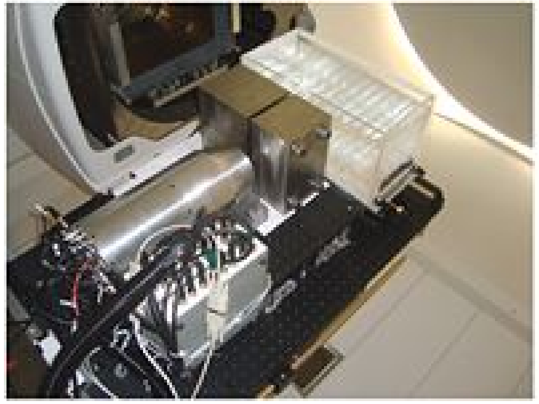
- Most promising approach nowadays
- Emission ~ns after irradiation.
- ~ 7 x more photons /cGy than positrons.
- Emitted in a continuous energy spectrum in the MeV range with characteristic peaks.

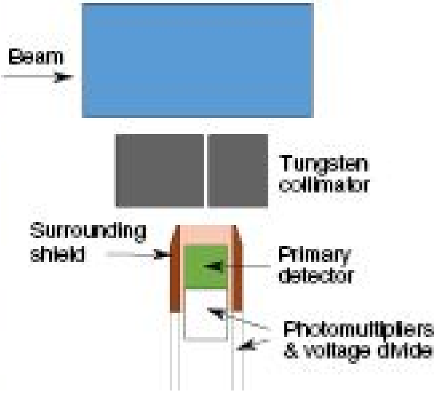




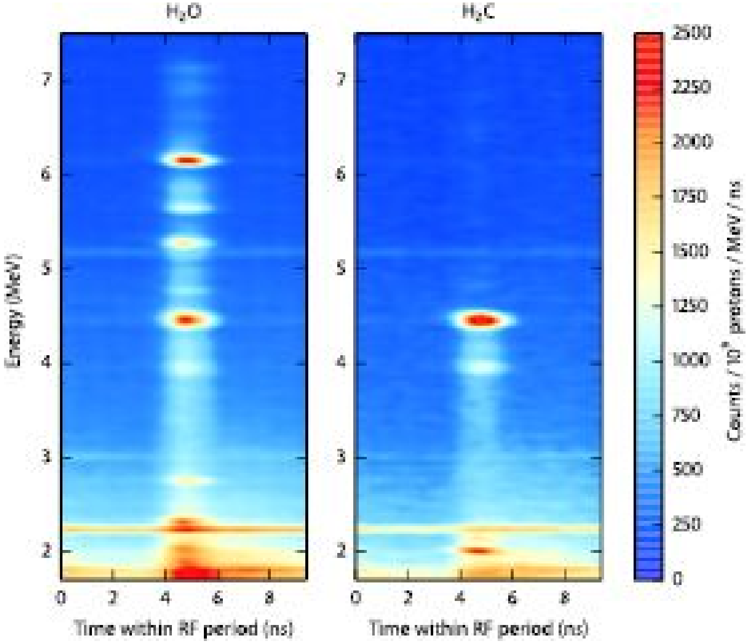
Prompt gamma spectroscopy

- 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.



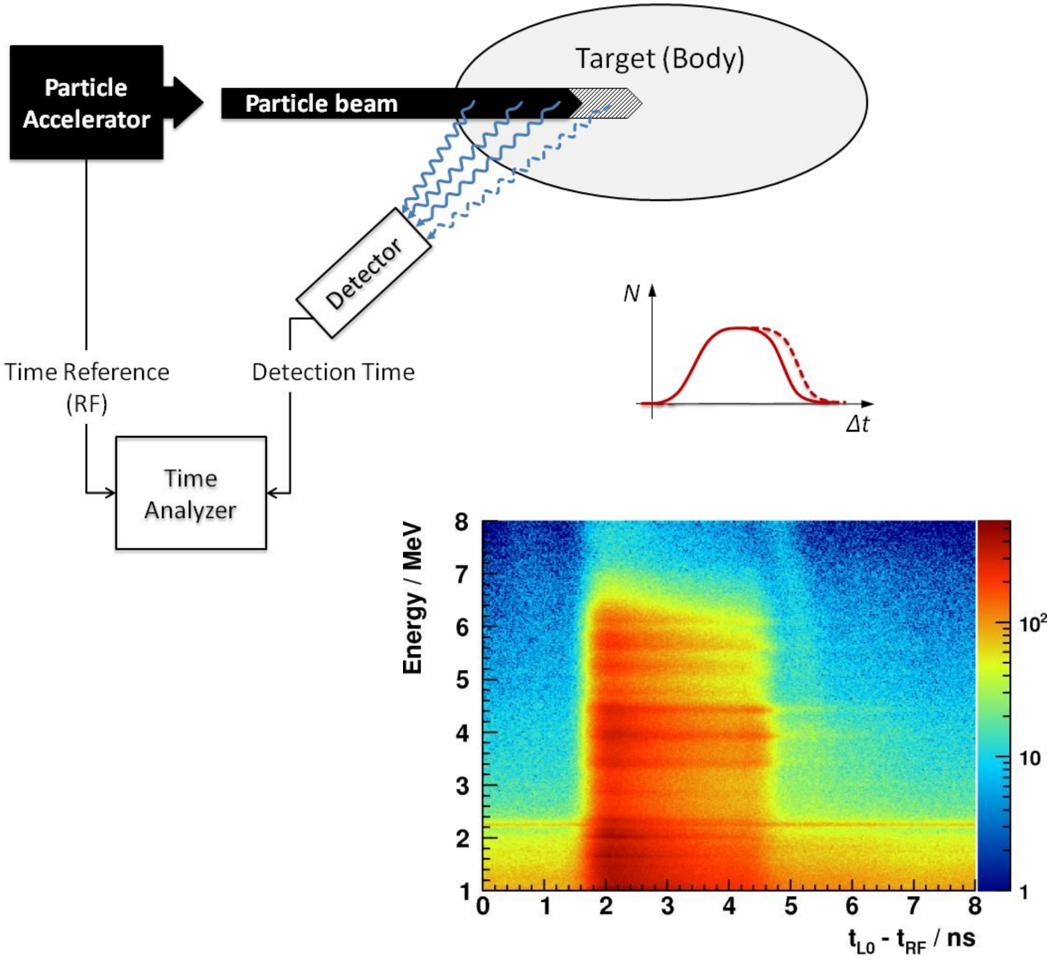


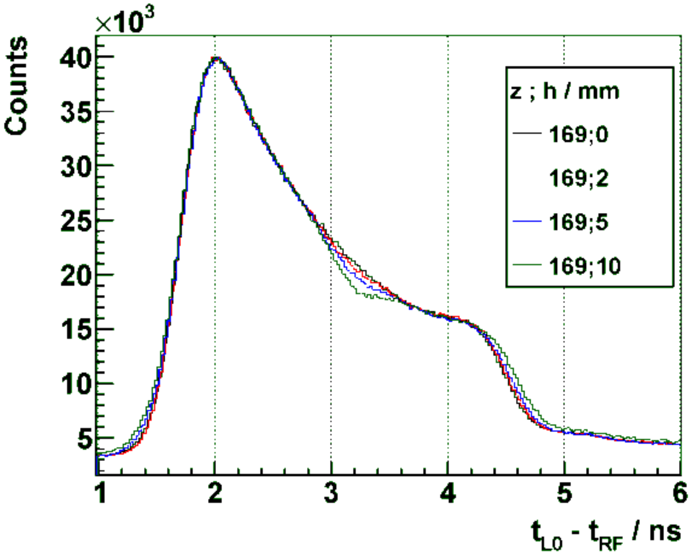
Verburg et al. PMB 58 (2013).



Prompt gamma timing

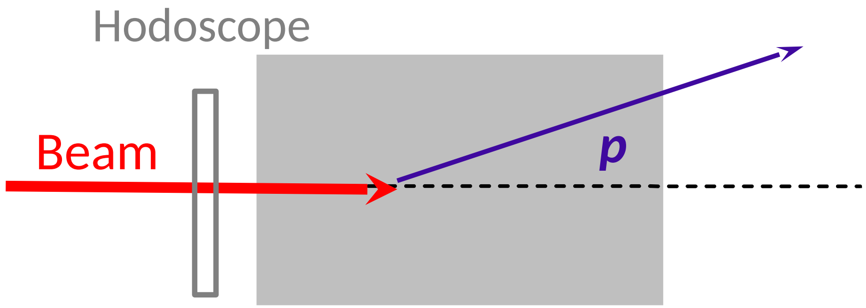
Gamma emission time is correlated with proton stopping time in the tissue, and thus with range.





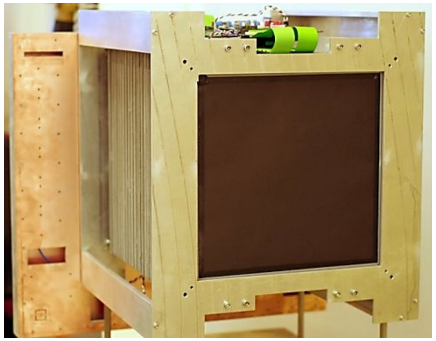
Hueso González et al., PMB 60 (2015) 6247.

Hodoscopes



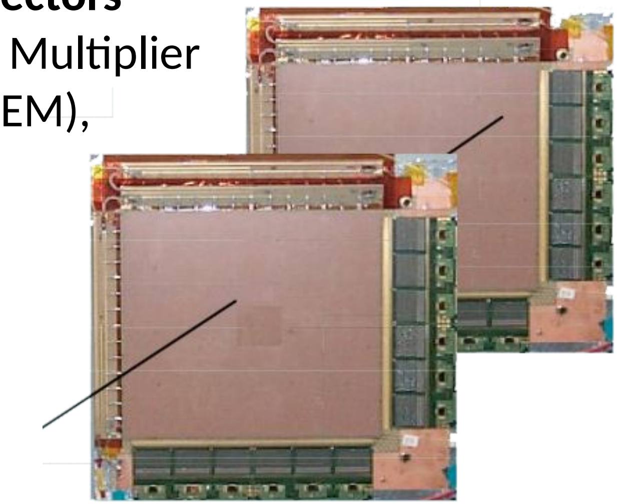
Silicon detectors: 4-plane proton tracker 2×2 cm^2. 12 µm Si-CMOS pixels , 50 µm thick ,

Plastic scintillators



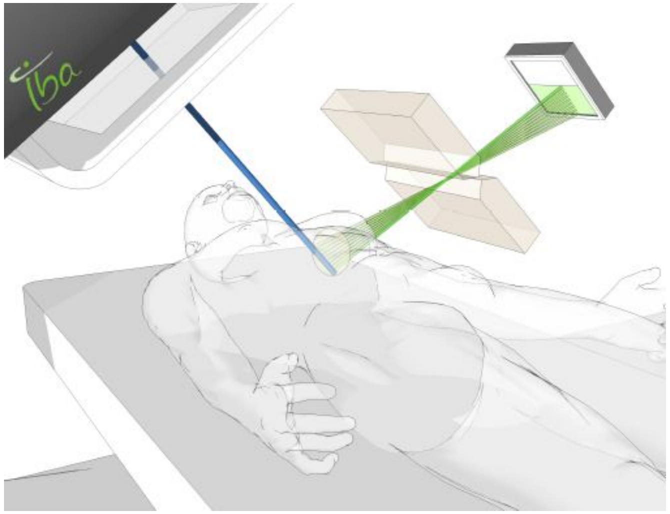
Scintillating fibers
128 +128 fibers

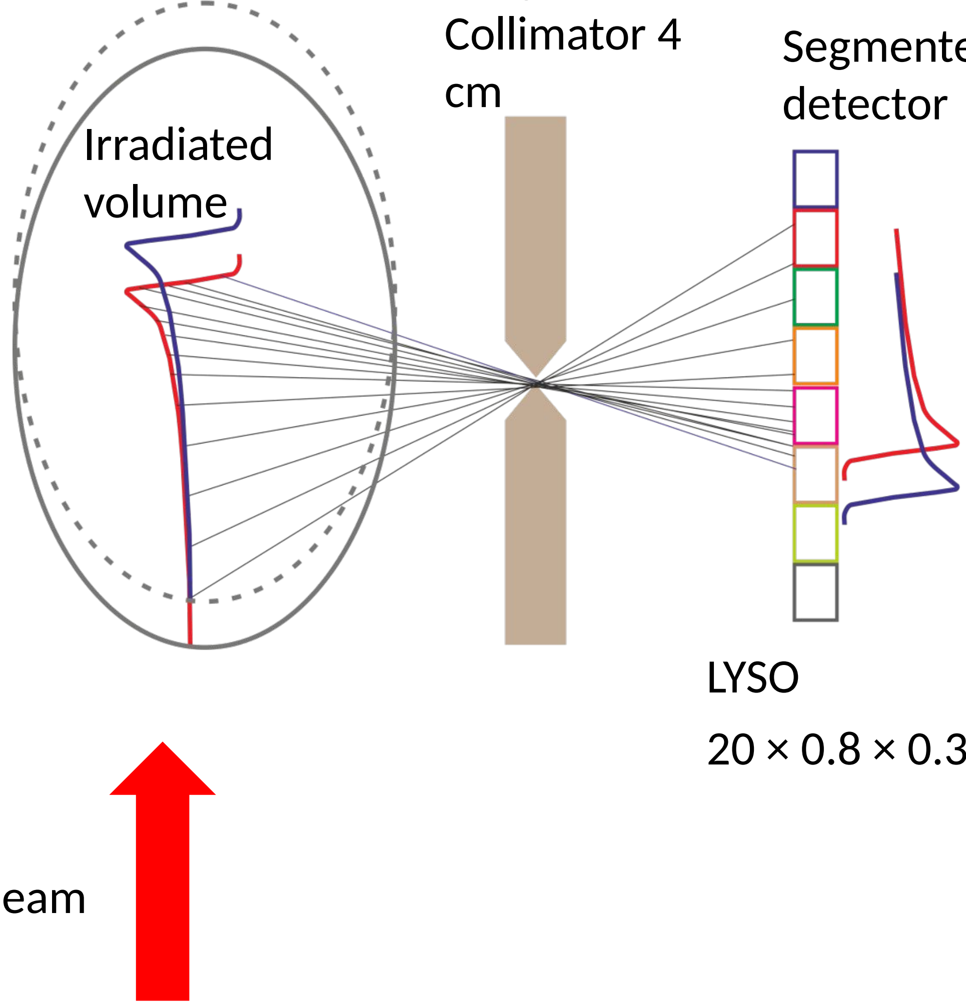
Gaseous detectors
Gas Electron Multiplier chambers (GEM), 30x30 cm^2 active area



Diamond detectors

Prompt gamma imaging with collimated cameras





Tungsten
Collimator 4
cm

Segmented
detector

Irradiated
volume

LYSO

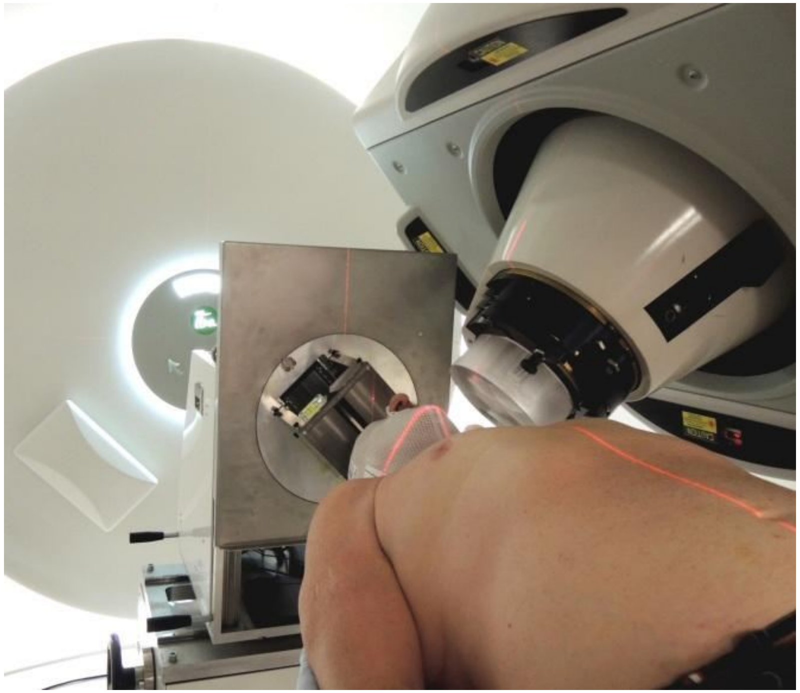
$20 \times 0.8 \times 0.32\ \text{cm}^3$

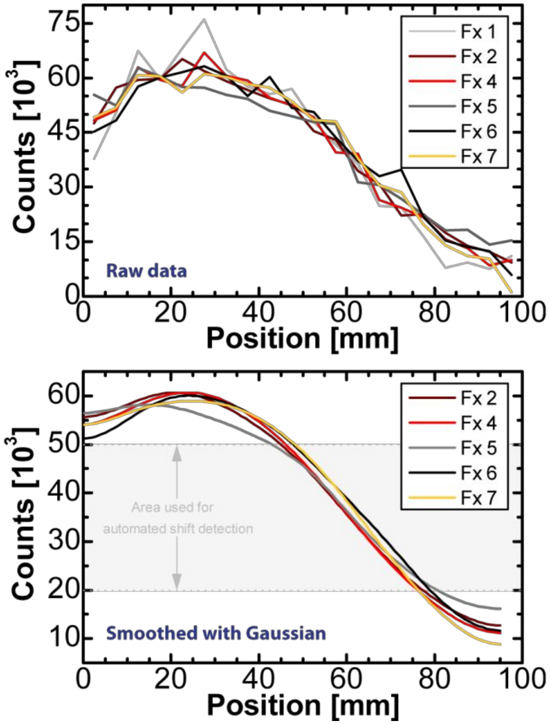
Beam

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

Prompt gamma imaging with collimated cameras

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

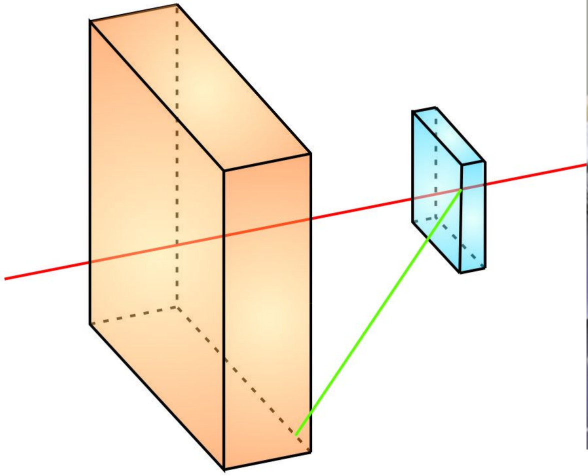


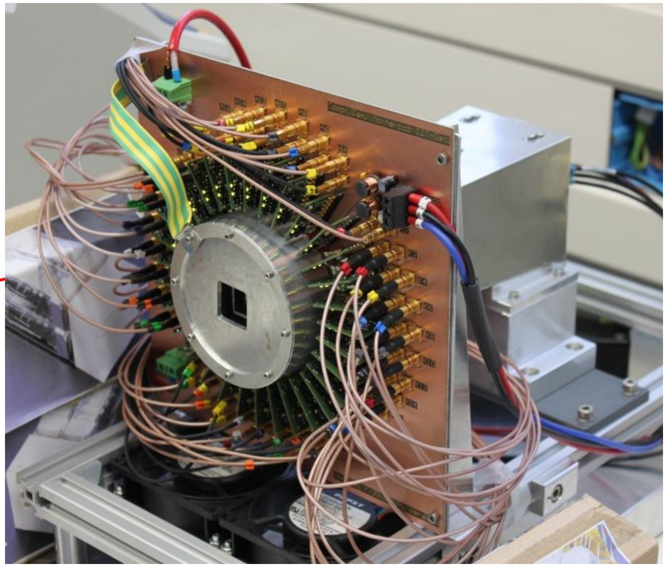


ΔR= [-2.0 mm,1.3 mm]

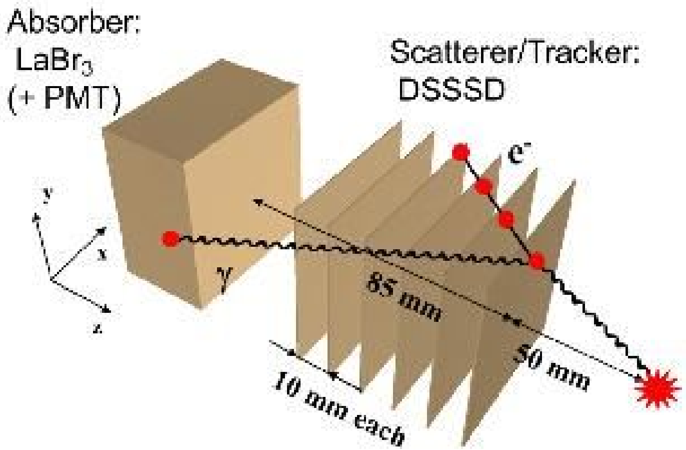
Prompt gamma imaging with Compton cameras

CZT + BGO

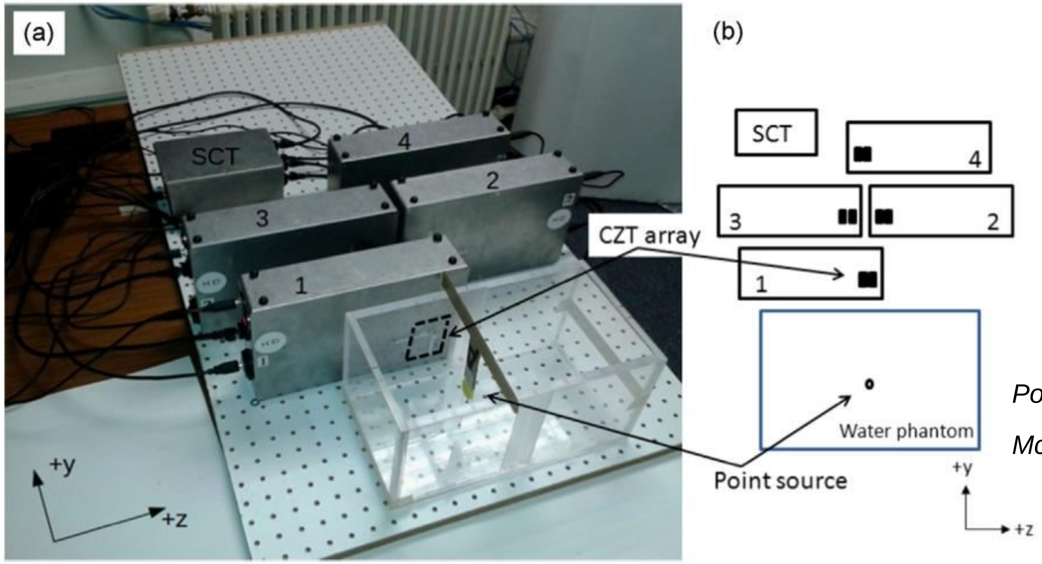




Thirolf et al., NN 2015



DSSD + LaBr$_3$



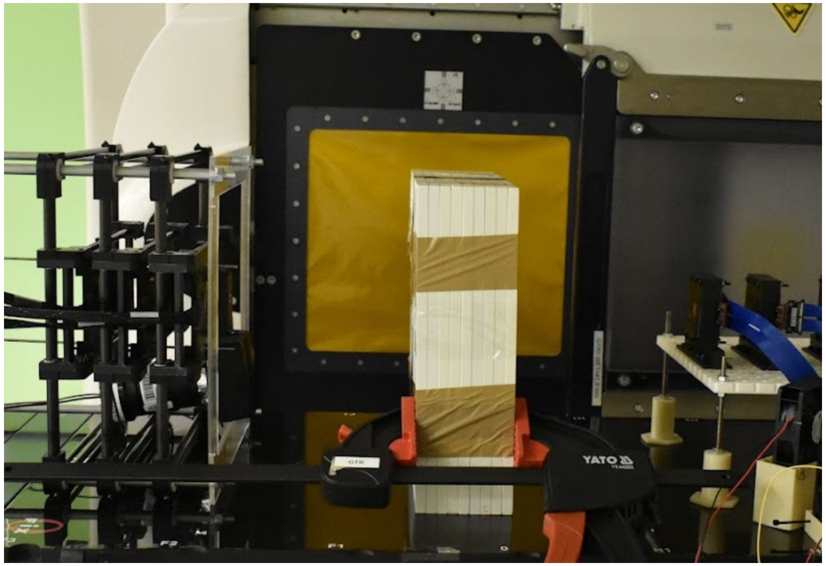
CZT

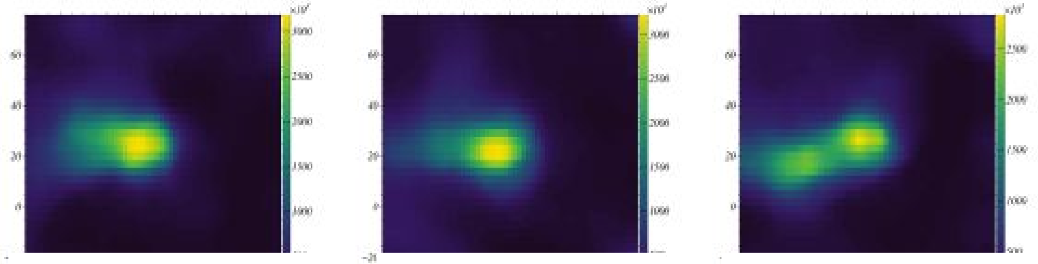
Polf et al., PMB 60 (2015) 7085

McCleskey et al., NIM A785 (2015) 163

Scintillator CCs

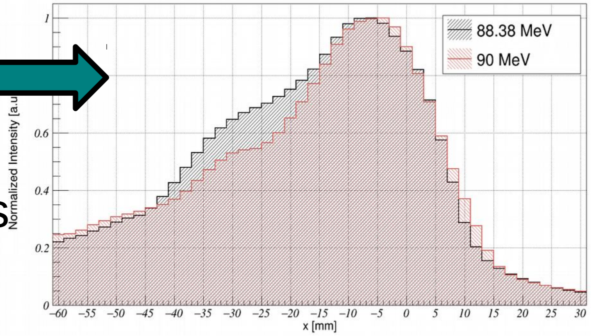
MACACO with LaBr3 detectors





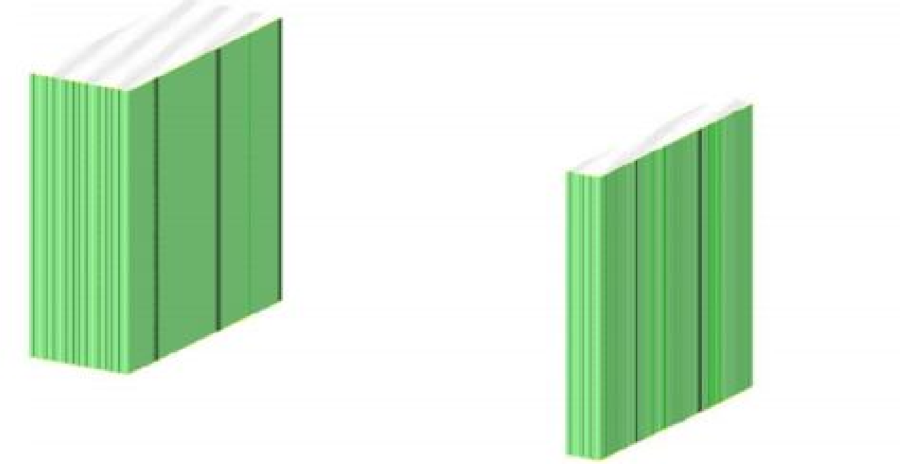
88.38 MeV 90 MeV 91.62 MeV

Proton beam at different energies

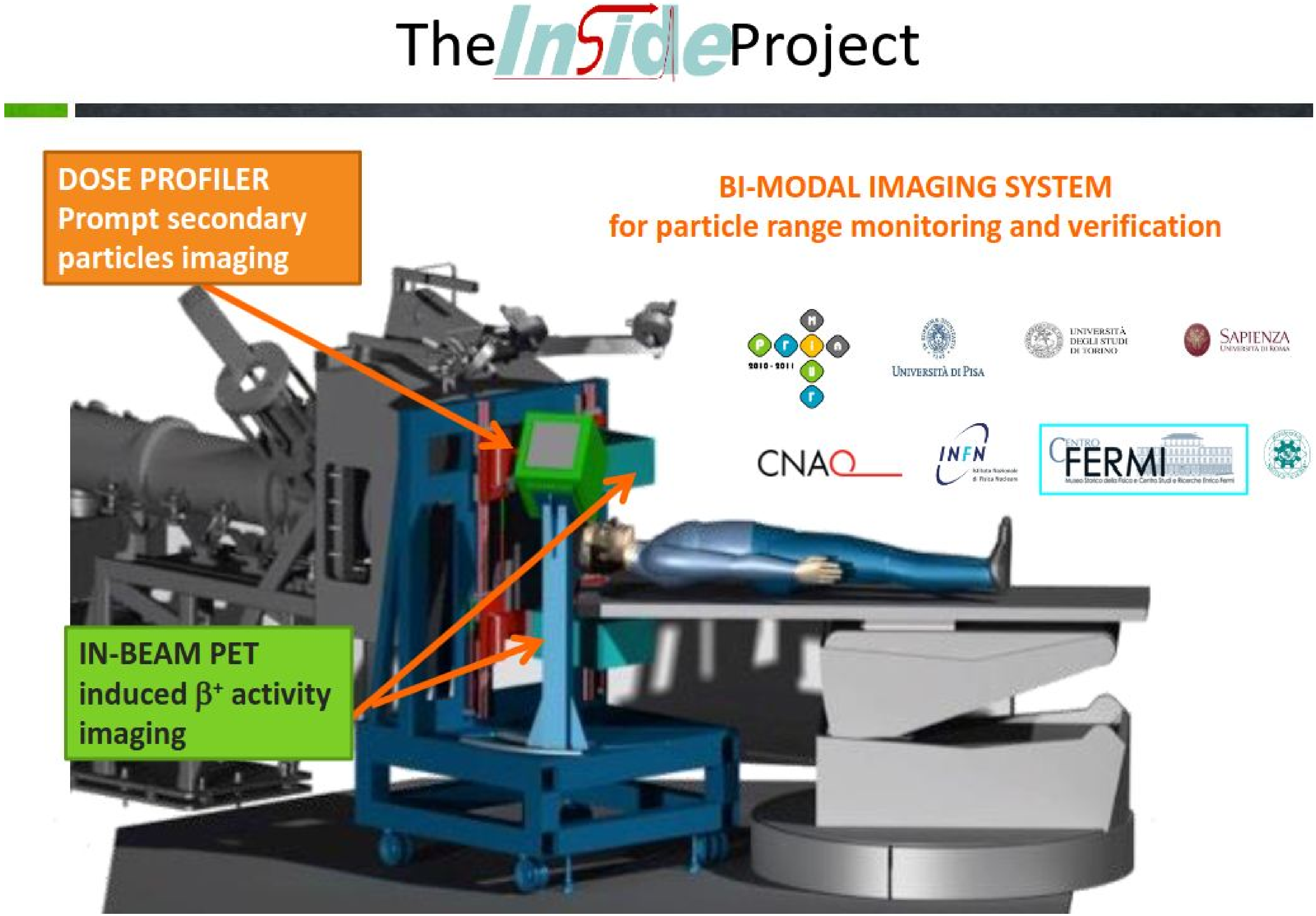


2 mm steps detected

SiFi- CC: Compton camera with scintillating fibers under development



Inside project



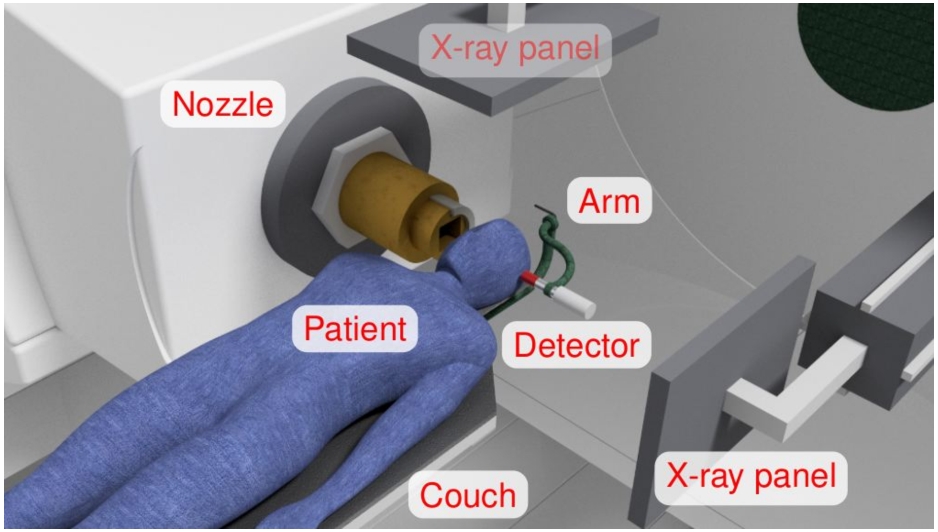
The InSide Project

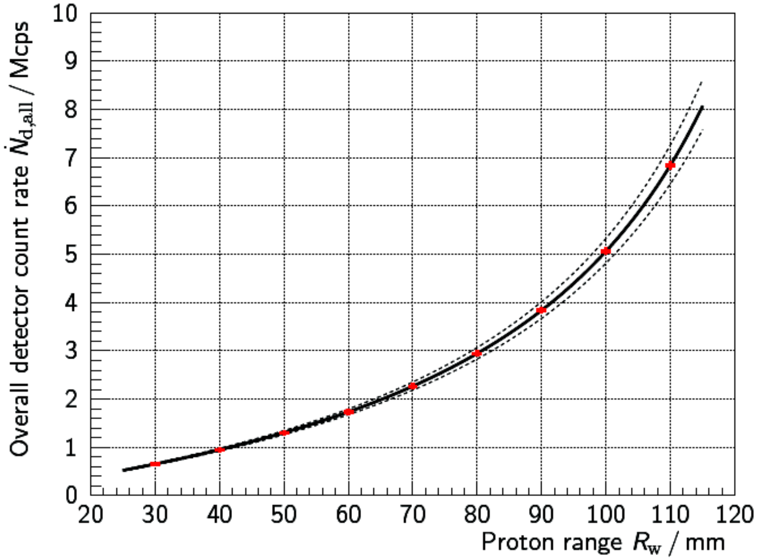
DOSE PROFILER
Prompt secondary particles imaging

BI-MODAL IMAGING SYSTEM
for particle range monitoring and verification

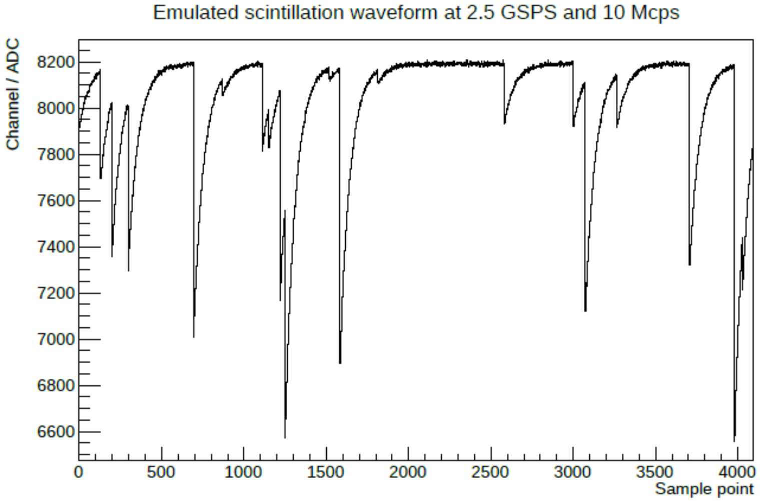
IN-BEAM PET
induced β^+ activity imaging

Coaxial Prompt gamma - ray monitoring





At 10 Mcps & 2.5 GSPS with a $\mathrm{CeBr_3}$ 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

Hadron therapy treatment monitoring

Unsolved problem

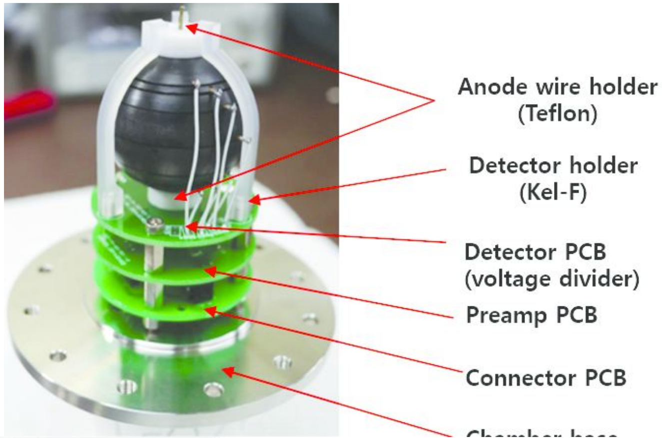
Challenging application

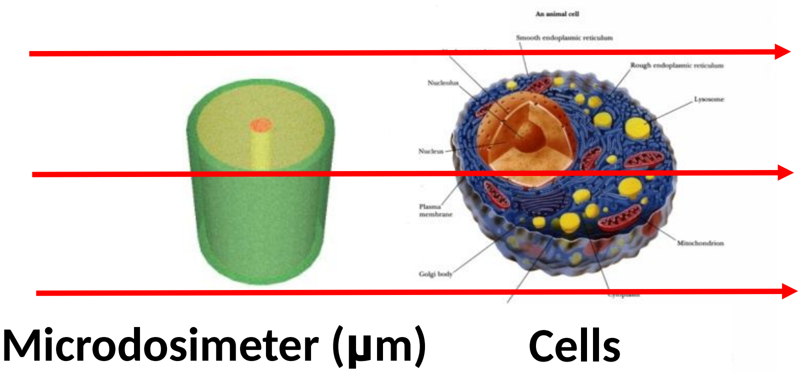
Even more challenging with modern synchrocyclotrons and flash therapy

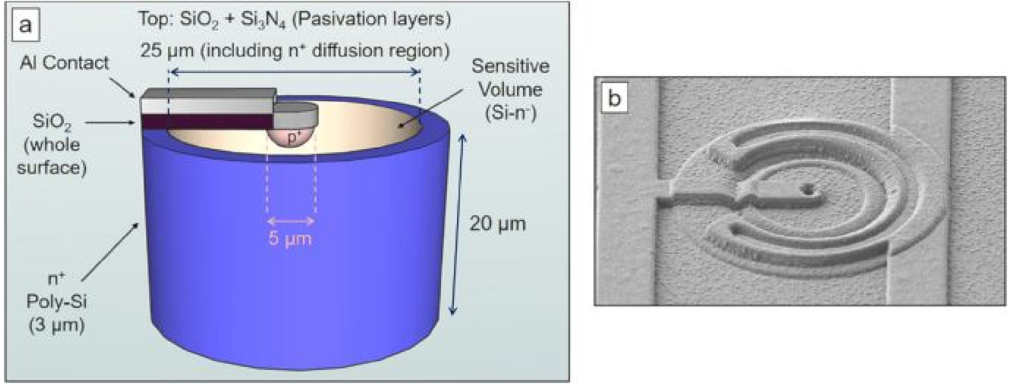
Needs to be compatible with treatment

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



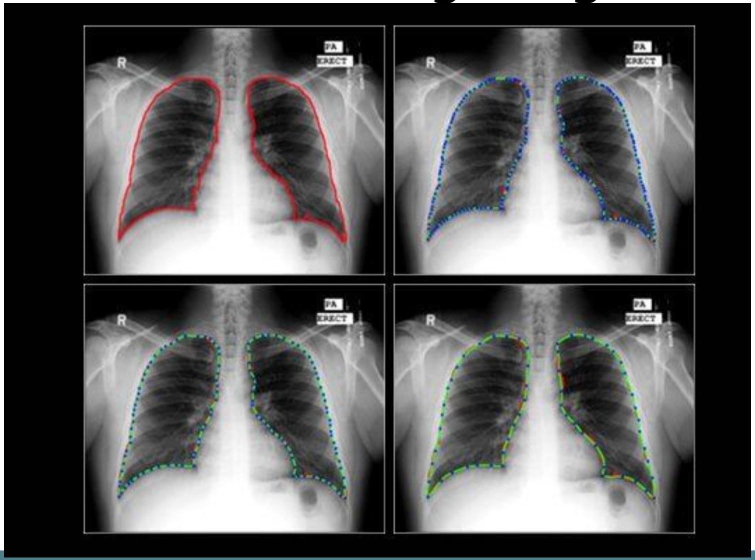




LET – Linear Energy Transfer
RBE – Relative Biological Effectiveness
TEPC- Tissue Equivalent Proportional Counter

And more….

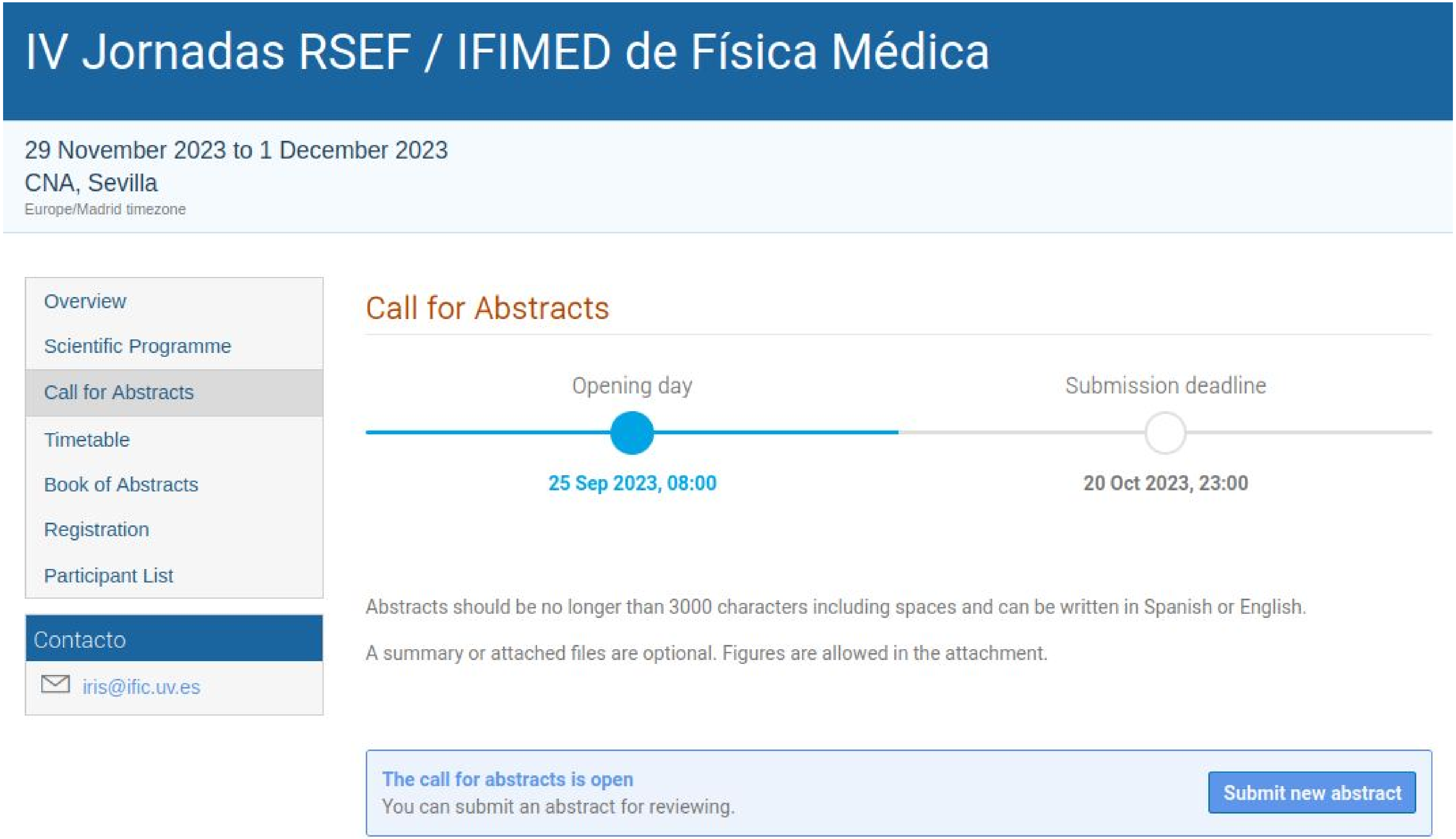
- Monte Carlo simulations: more accurate, faster.
- Artificial Intelligence:
  - Facilitate detection and quantification of a wide array of clinical conditions - radiomics.
    - Well established in diagnostics.
    - Increasing prognosis, screening, therapy response assessment and prediction
  - Data analysis: position / energy determination, background reduction, denoising, segmentation,….



Conclusions

- Many aspects in which the performance of medical imaging devices can be improved.
- Nuclear and HEP have the capacity to contribute to this field.
- Necessary contact with hospitals / specialized groups to know what the requirements are and to address properly the needs.

Medical Physics Days. CNA, Sevilla 29 Nov-1 Dec



IV Jornadas RSEF / IFIMED de Física Médica

29 November 2023 to 1 December 2023
CNA, Sevilla
Europe/Madrid timezone

Call for Abstracts

Opening day: 25 Sep 2023, 08:00

Submission deadline: 20 Oct 2023, 23:00

Abstracts should be no longer than 3000 characters including spaces and can be written in Spanish or English.

A summary or attached files are optional. Figures are allowed in the attachment.

The call for abstracts is open
You can submit an abstract for reviewing.

Organized by GEFM from the Spanish Royal Physics Society RSEF & CNA (M.C. Jiménez)

Acknowledgements

- MCIN /AEI (PID2019-110657RB-I00).
- MCIN /AEI 10.13039/501100011033 (PDC2021-121839-I00).
- MCIN with funding from the European Union NextGenerationEU (PRTR-C17.I1) and Generalitat Valenciana. Proj. ICOR, ref. ASFAE/2022/019
- Generalitat Valenciana, Prometeo CIRPOM/2022/70.

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Thank you

Gabriela.llosa@ific.uv.es

http://ific.uv.es/iris