PET technique and applications

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The PHYSICS of PET

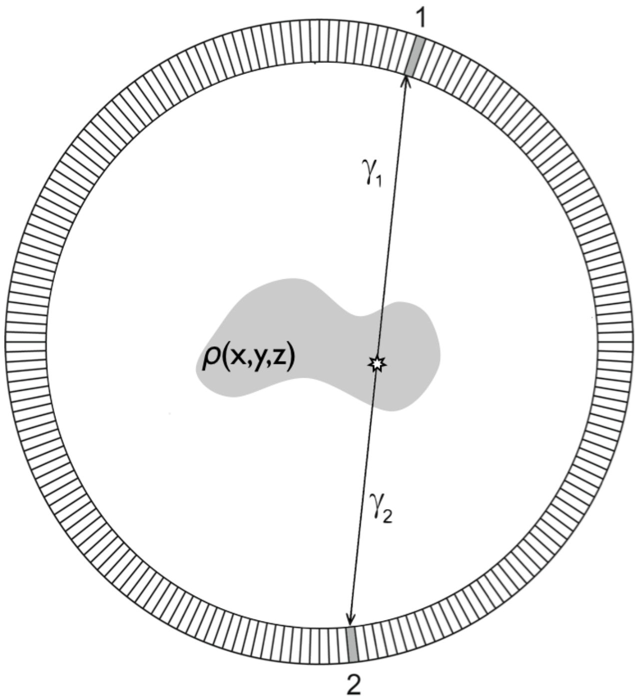
The radioactive decay

- Isotope decays, emitting β^+.

^{18}F	2 hour half-life
^{15}O, ^{11}C, ^{13}N	2–20 minute half-life

- β^+ annihilates with e^- from tissue, forming back-to-back 511 keV photon pair.
- 511 keV photon pairs detected via time coincidence.
- Positron lies on line defined by detector pair (Line of FLIGHT =LOF ➔ LOR).

The annihilation process



The collinear emission of an annihilation γ-ray pair defines the Line-Of-Flight (LOF). The LOFs are collected by surrounding the object with a "ring" of detectors.

The activity distribution ρ(x,y,z) is measured in terms of projections ($N_{\gamma-\gamma}$) along lines L.
Each projection is obtained from the activity distribution with the line integral operator:

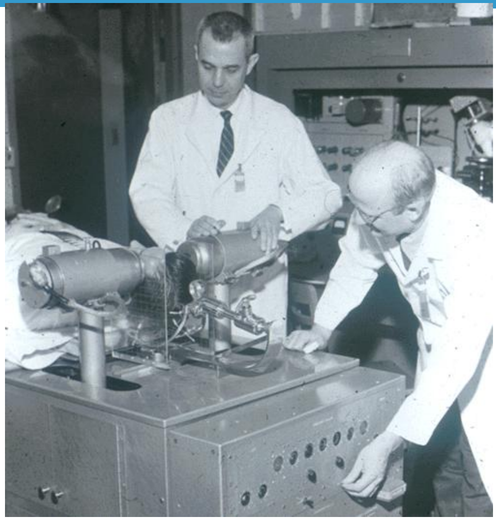
$$N_{\gamma-\gamma} = k \int_L \rho(x,y,z)\, dl$$

The TECHNOLOGY of PET

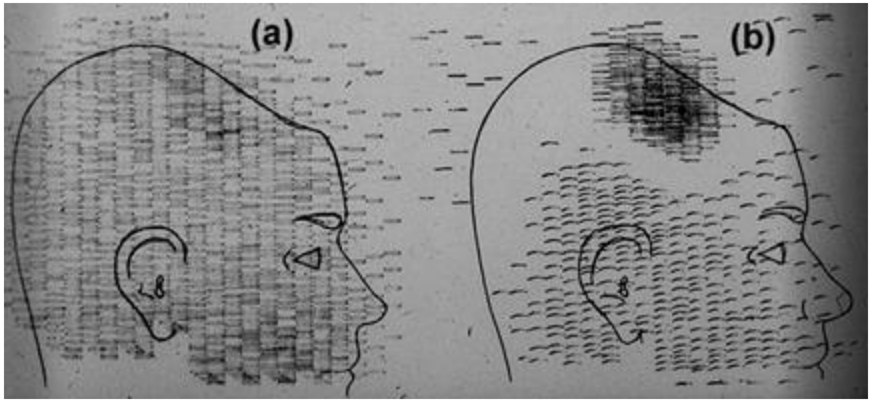
50's - The beginning of PET / 1

First Clinical Positron Imaging Device

1952 - This instrument followed the general concepts of the instrument build in 1950 but included many refinements. It produced both a coincidence scan as well as an unbalance scan. The unbalance of the two detectors was used to create an unbalance image using two symbols to record any unbalance in the single channel rates of the two detectors.

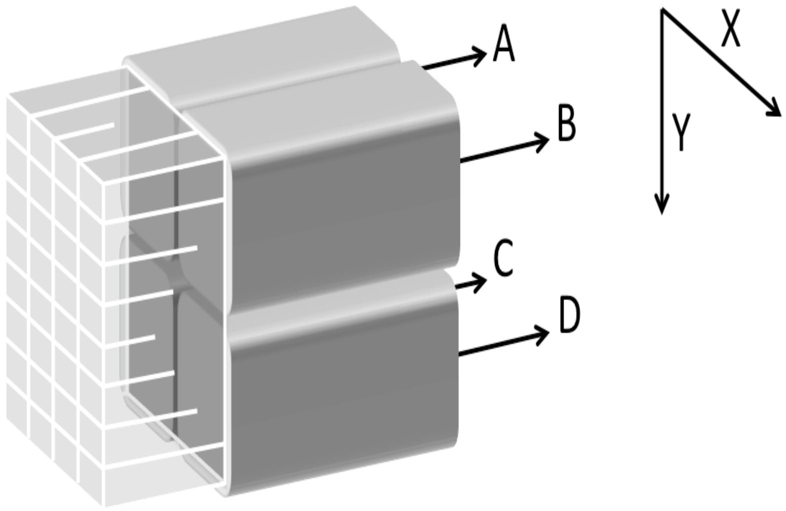


Dr. Brownell (left) and Dr.Aronow are shown with the scanner (1953).



Coincidence and unbalance scans of patient with recurring brain tumor. Coincidence scan (a) of a patient showing recurrence of tumor under previous operation site, and unbalance scan (b) showing asymmetry to the left. (Reproduced from Brownell and Sweet 1953).

The block detector (*)



Scheme of a Block Detector.

A block of scintillator is subdivided by cuts at different depths into 4×8 rectangular elements.

The block is read out by a matrix of 2×2 photomultiplier tubes (outputs S_A, S_B, S_C and S_D).

(*) **Casey M.E., Nutt R. *IEEE Trans. Nucl. Sci.* 33, n° 1 (1986): 460-463.**

Properties of the Scintillators (*)

	NaI	BGO	GSO	LSO	LYSO	LGSO	LuAP	YAP	$LaBr_3$
Light yield 10^3 ph/MeV	38	9	8	30	32	16	12	17	60
Primary decay time	250	300	60	40	41	65	18	30	16
ΔE/E (%) at 662 keV	6	10	8	10	10	9	15	4.4	3
Density (g/cm^3)	3.67	7.13	6.71	7.35	7.19	6.5	8.34	5.5	5.08
Effective Z_{eff}	50	73	58	65	64	59	65	33	46
1/μ @ 511 keV (mm)	25.9	11.2	15.0	12.3	12.6	14.3	11.0	21.3	22.3
PE (%) at 511 keV	18	44	26	34	33	28	32	4.4	14

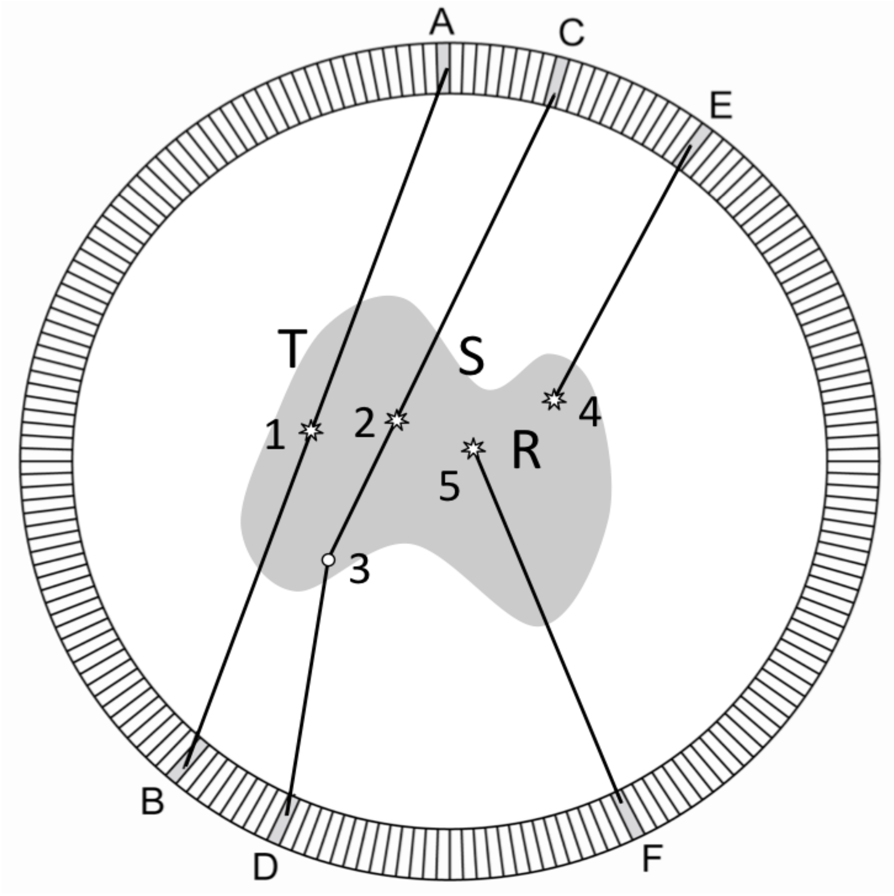
(*) **Adapted from Lecomte R. *Eur J Nucl Med Mol Imaging* 36, n° Suppl. 1 (2009): S69–S85.**

Spatial Resolution

$$FWHM = 1.2\sqrt{\left(\frac{d}{2}\right)^2 + b^2 + (0.0022D)^2 + r^2 + p^2}$$

1.2	**from analytical algorithm (FBP)**
d/2	**from the detector pitch**
b	**from the coding**
0.0022D	**from the 2 photons a-collinearity**
r	**from the positron range**
p	**from parallax**

Sensitivity: NOT all events are good events!
True (T), Scatter (S) and Random (R) events.



A true coincidence is generated in point 1 and the annihilation photons are detected in opposing crystals A and B.

A Scatter coincidence is generated in point 2 and one annihilation photon is detected in crystal C while the other is detected in opposing crystal D after a Compton scattering interaction in 3.

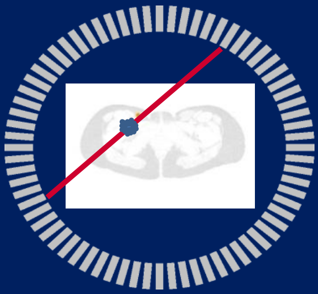
A random coincidence is detected in opposing crystals E and F for two annihilations in 4 and 5 occurring with a time difference shorter that the coincidence window.

TOF systems: signal to noise ratio

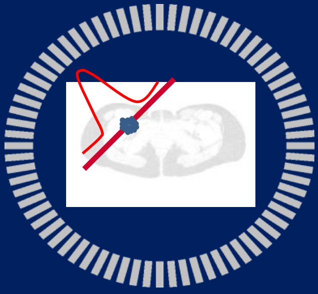
The gain in terms of SNR of the images acquired with TOF-PET systems is proportional to the object dimensions and inversely proportional to the time resolution.

$$SNR_{TOF} \approx \sqrt{\frac{2D}{c\Delta t}} \cdot SNR_{non-TOF}$$

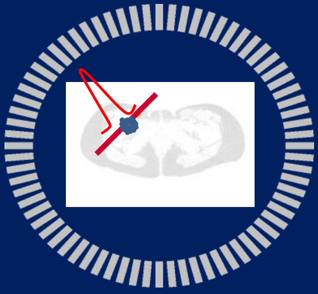
D= diameter of the acquired object
c= light speed
Δt= time resolution



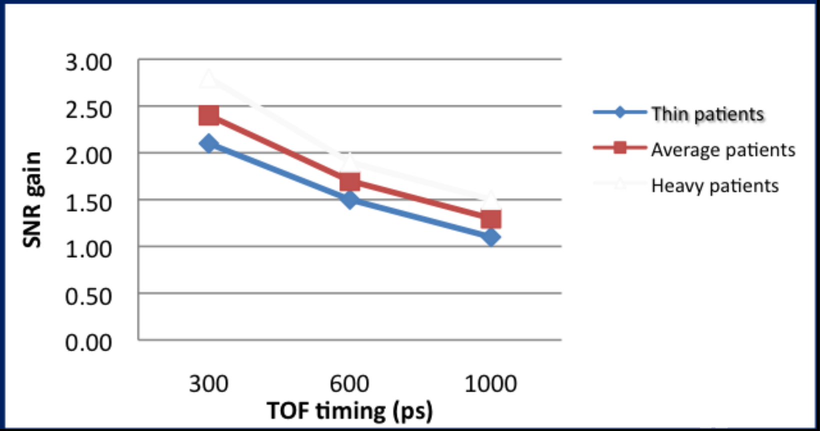
no TOF



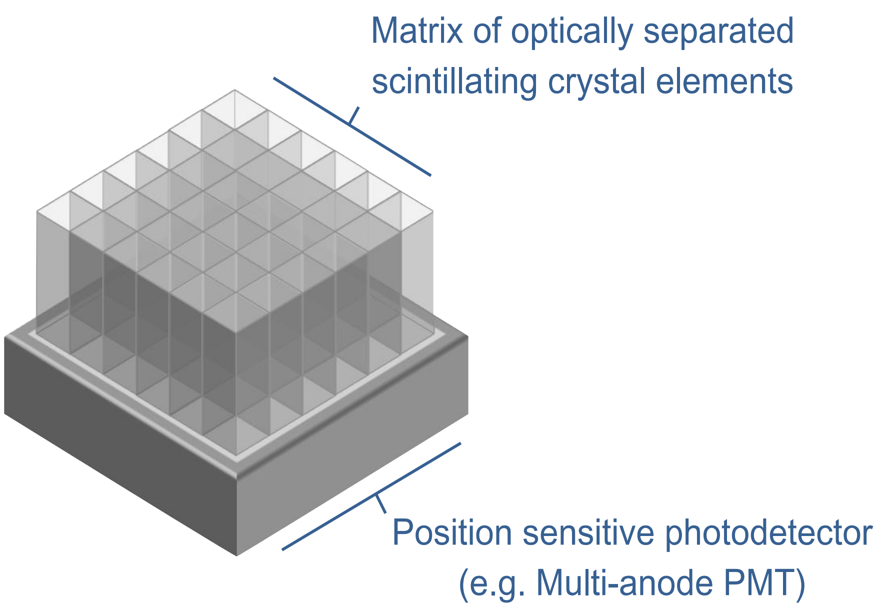
TOF 600 ps



TOF 300 ps



Increasing Spatial Resolution

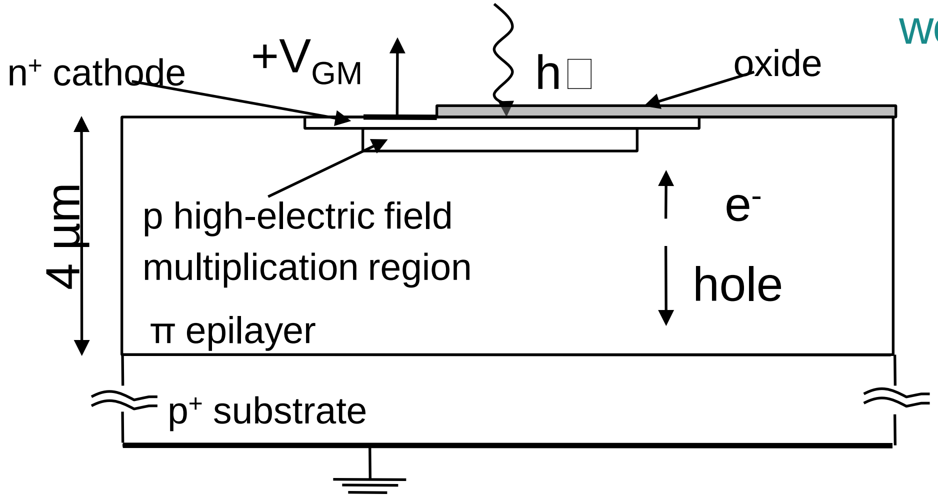


Left: A possible configuration of a PET detector comprised of a MA-PMT and a matrix of scintillating crystals. In this case, the pixel size contribution in the spatial resolution formula is *d*/2 while the coding factor is *b*>0.

Right: The popular Hamamatsu H8500 with 8 × 8 independent anodes. Its main features are minimum peripheral dead zone (1 mm) and minimal height (12 mm).

Silicon PhotoMultiplier = SiPM
The Ultimate dream??

SOLID STATE PHOTODETECTOR➔



-The photon is absorbed and generates an electron/hole pair

-The electron/hole diffuses or drifts to the high-electric field multiplication region

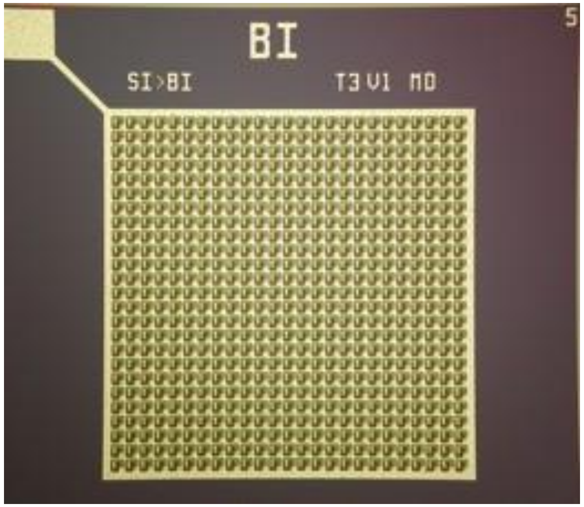
-The drifted charge undergoes impact ionization and causes an avalanche breakdown.

-Resistor in series to quench the avalanche (limited Geiger mode).

As produced at FBK-irst,Trento, Italy➔

SiPM: **Multicell Avalanche Photodiode** working in limited Geiger mode

- 2D array of microcells: structures in a common bulk.
- Vbias > Vbreakdown: high field in multiplication region
- Microcells work in Geiger mode: the signal is independent of the particle energy
- The SiPM output is the sum of the signals produced in all microcells fired.



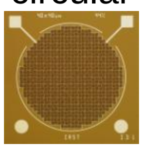
➔High gain ➔Low noise ➔ Good proportionality if $N_{photons} << N_{cells}$

Development of detectors geometry (May 2007)

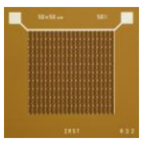
Different geometry,size,microcell size and GF.

40x40μm² => GF 44%
50x50μm² => GF 50%
100x100μm² => GF 76%

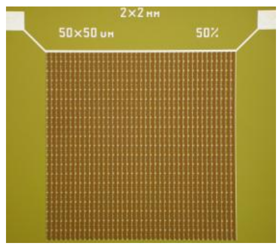
circular



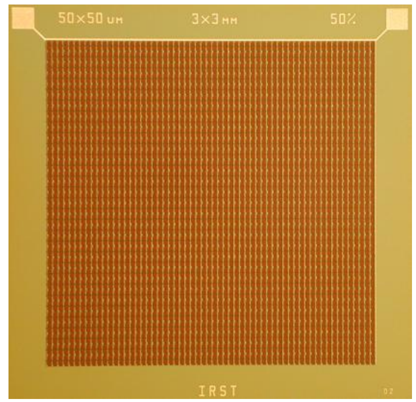
1mm ϕ



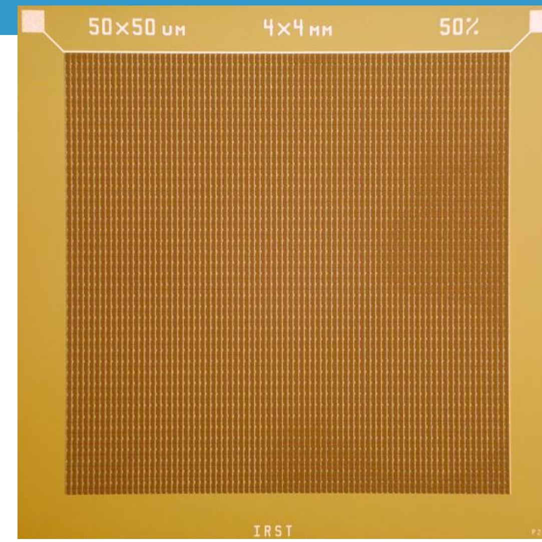
1x1mm²



2x2mm²

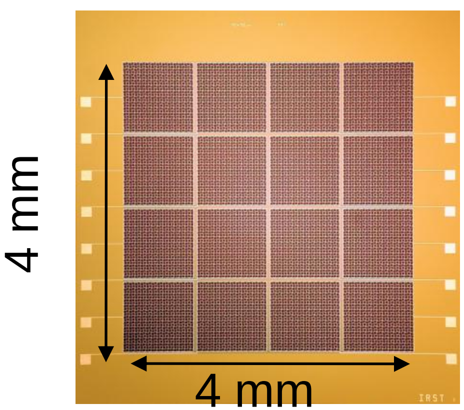


3x3mm² (3600 cells)



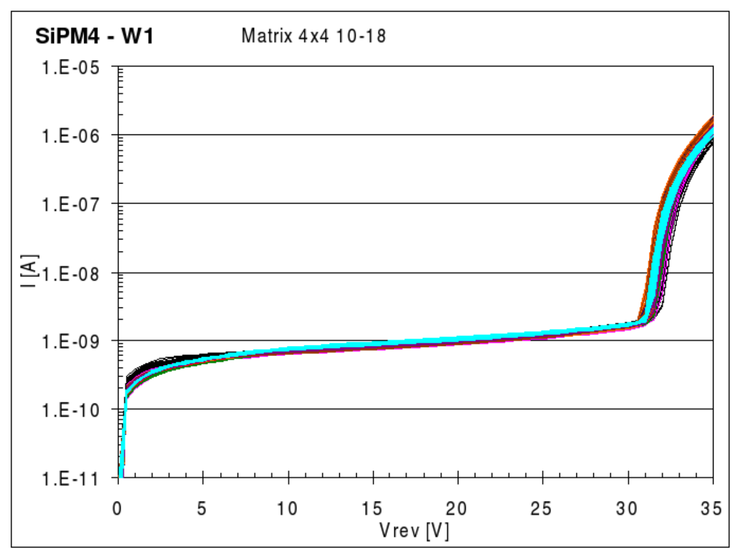
4x4mm² (6400 cells)

Matrices 16 elements (4x4)



IV CURVES OF 9 MATRICES.

VERY UNIFORM BREAKDOWN POINT



[C.Piemonte et al, Il Nuovo Cimento C, 2007,30(5),473-482]

PET in MEDICAL IMAGING
➔MOLECULAR IMAGING

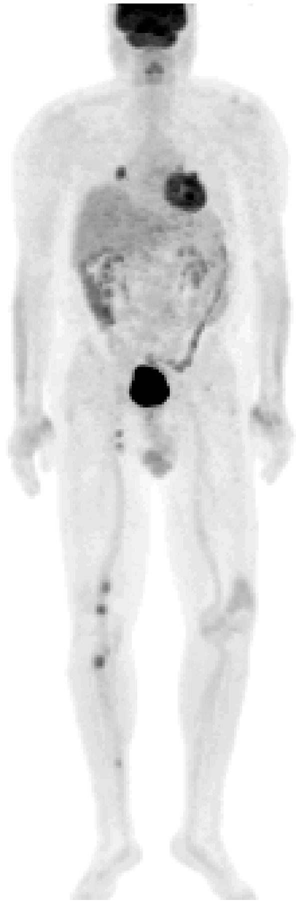
"A *visual representation,characterization, and quantification of biological processes at the cellular and subcellular levels within intact living organisms."*

Sanjiv S.Gambhir

CLINICAL SYSTEMS
Hybrid Systems – PET/CT

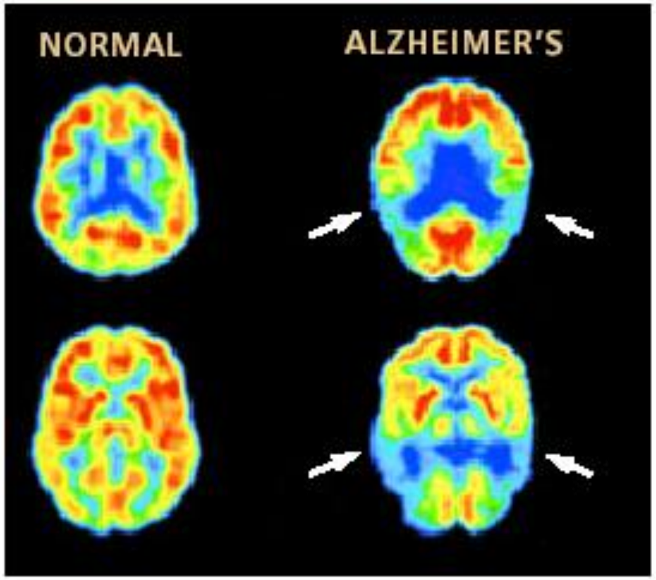
Clinical PET applications

Oncology

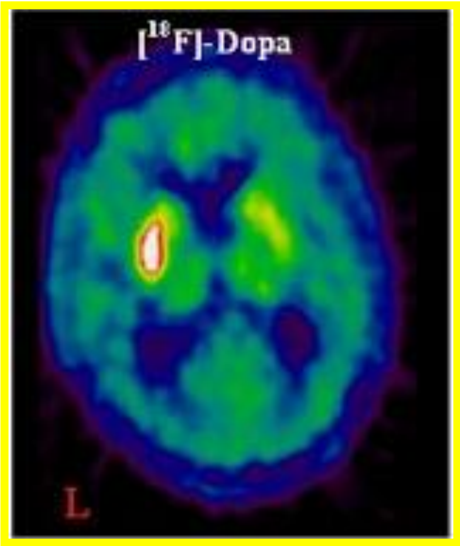


^{18}F-FDG
Total body

Neurology



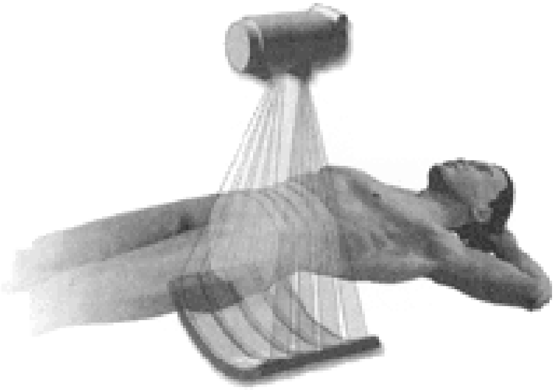
^{18}F-FDG
Brain study for
Alzhemeir's disease

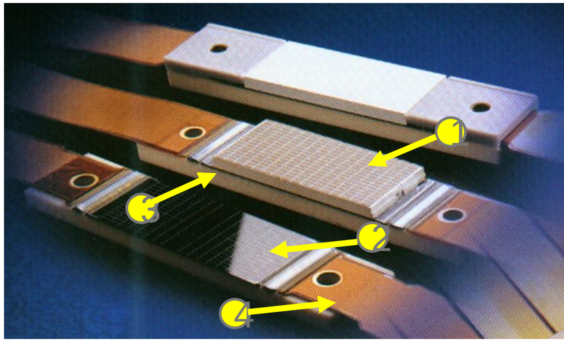


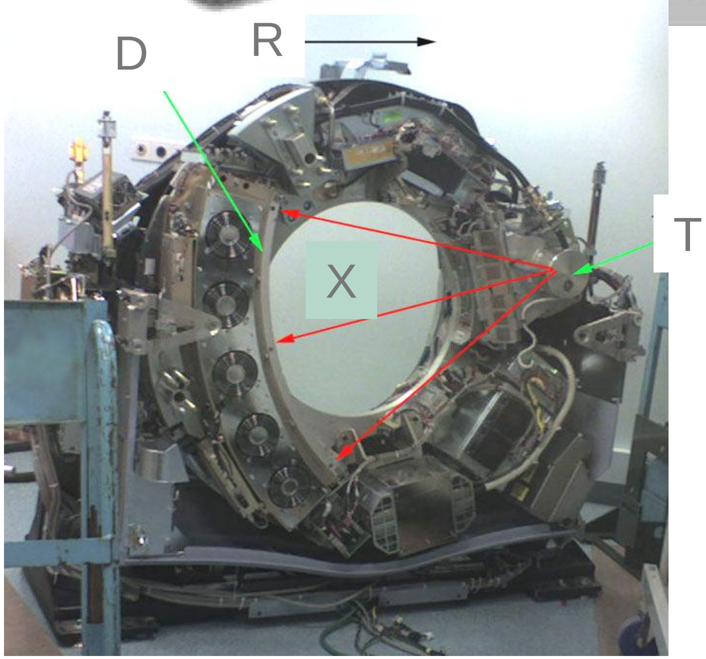
^{18}F-DOPA
Brain study for
Parkinsons's disease

CT technology

- **Spiral CT (With multirow detectors) (> 1998).**



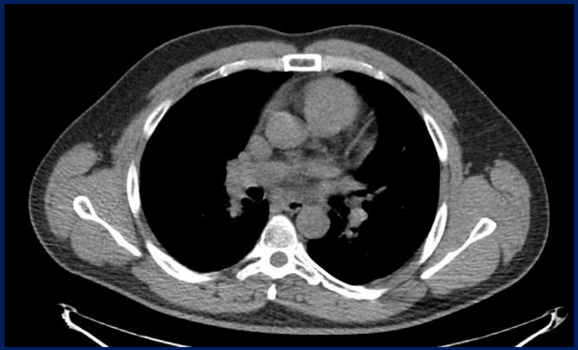


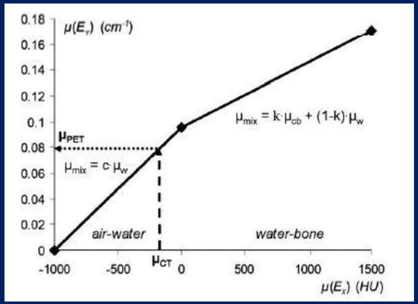


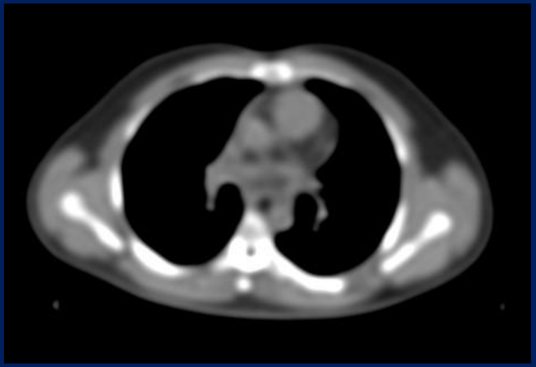
Attenuation correction

- PET needs CT data to anatomically locate the tumor and to correct for the attenuation in order to provide a correct quantification.

- Present systems exploit multislice CT top quality systems, where the number of slices can achieve 128 with rotation time of the order of 300 ms.







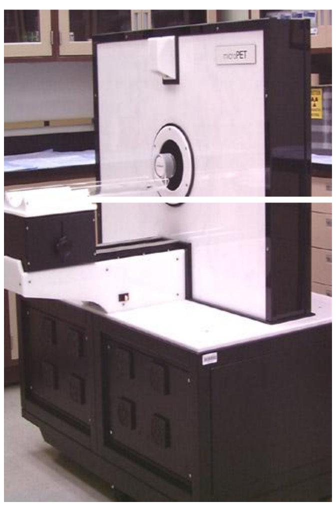
Being the attenuation coefficients (μ) energy dependent, the CT scanning at an average energy of 70 keV must be rescaled (voxel by voxel) to the gamma rays by using a bi-linear scaling function.

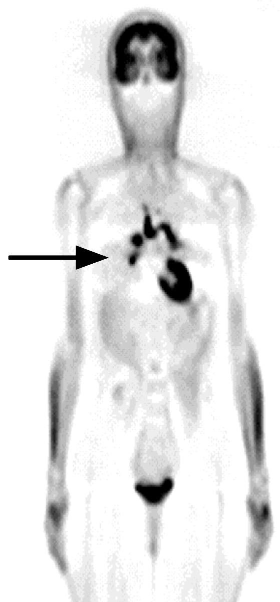
PRECLINICAL SYSTEMS
Hybrid Systems – PET/CT

“From man to mice” …

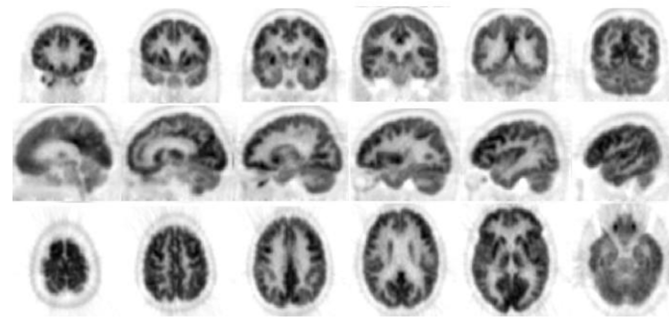
Human PET

microPET





human

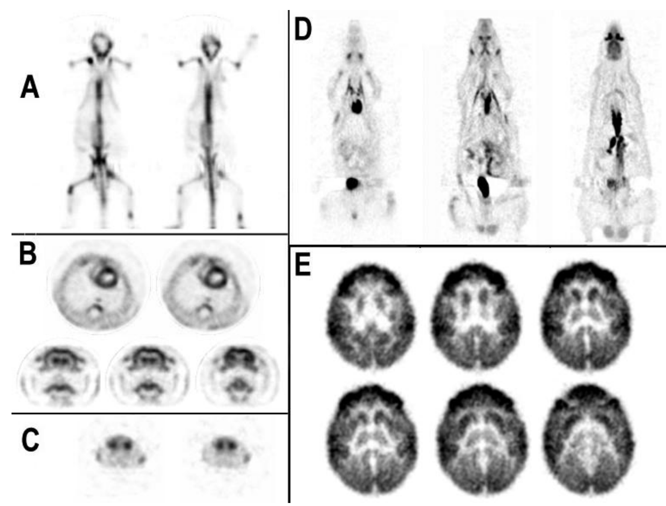


*Images courtesy of Simon Cherry, UCLA

mouse

rat

mouse

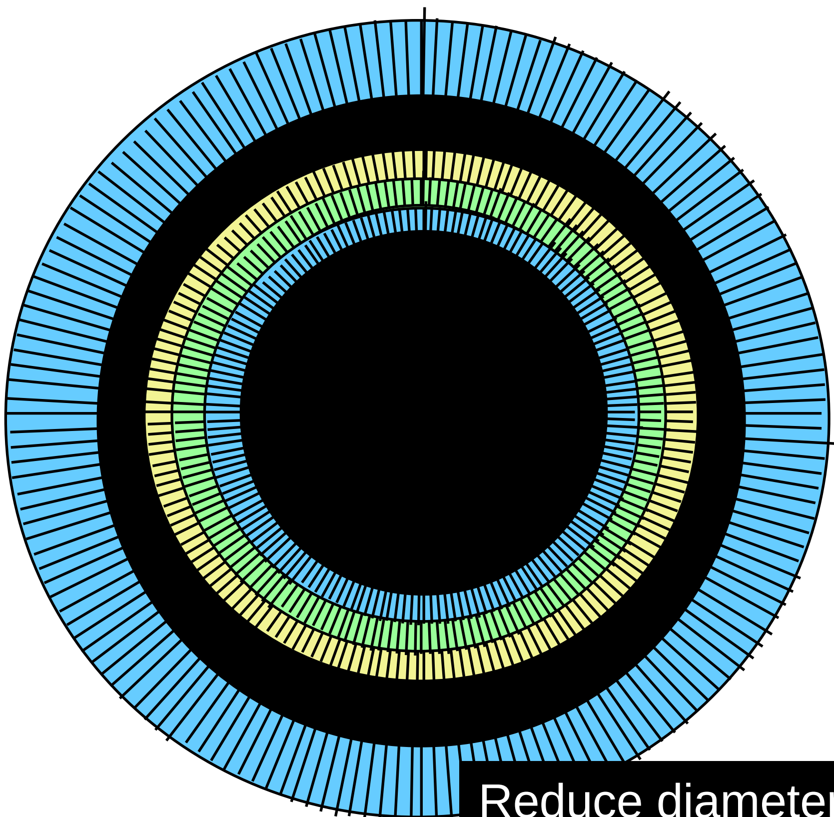


rat

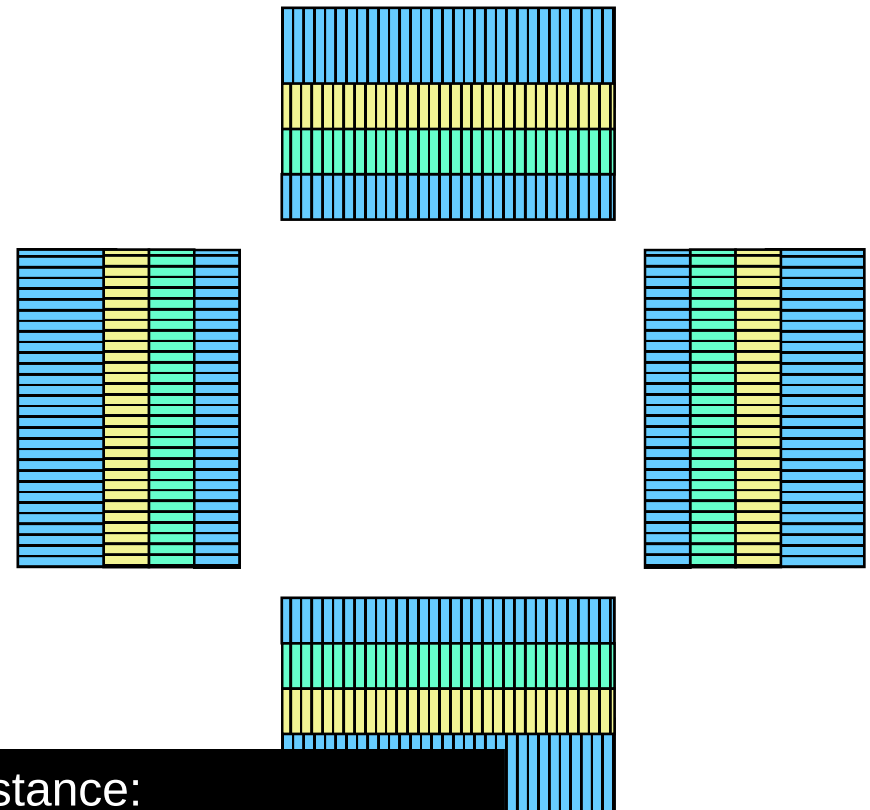
infant monkey

Sensitivity vs Resolution tradeoff

Stationary ring geometry



Rotating planar geometry



Reduce diameter / distance:

• Increase solid angle coverage

• Less crystals

• Thinner crystals for reducing parallax error

Increase thickness with DOI capability for increasing sensitivity

• Thick scintillator for h ... gh efficiency

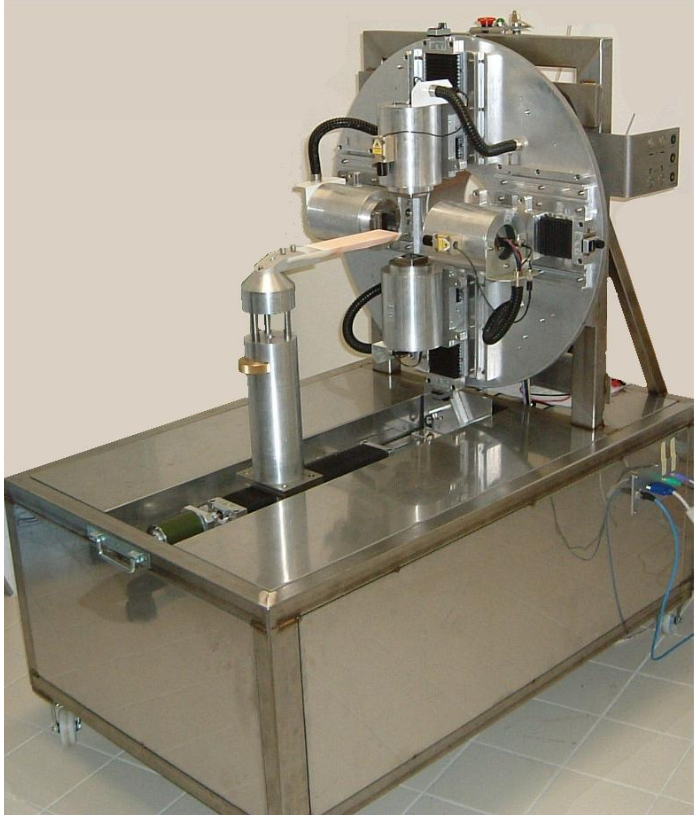
• Radial elongation due ... ation due to parallax

Technology transfer I: YAP-(S)PET small animal scanner (ISE, Italy)

yap (s)pet II by FIIG
FUNCTIONAL IMAGING AND INSTRUMENTATION GROUP
UNIVERSITY OF PISA

Scanner configuration

Configuration:	**Four rotating heads**
Scintillator:	$YAlO_3$:Ce (YAP:Ce)
Crystal size:	27 x 27 (1.5 x 1.5 x 20 mm^3 each)
Photodetector:	Position Sensitive PMT
Readout method:	Resistive chain (4 channels)
FoV size:	40.5 mm axial × 40.5 mm Ø
Collimators (SPECT):	Lead (parallel holes)
Head-to-head distance:	10-15 cm



The YAP-(S)PET Scanner is installed at the "Institute of Clinical Physiology" (IFC-CNR) within the framework of the **Center of Excellence AmbiSEN** of the **University of Pisa, Italy**

Small animal CT Xalt$_{HR}$

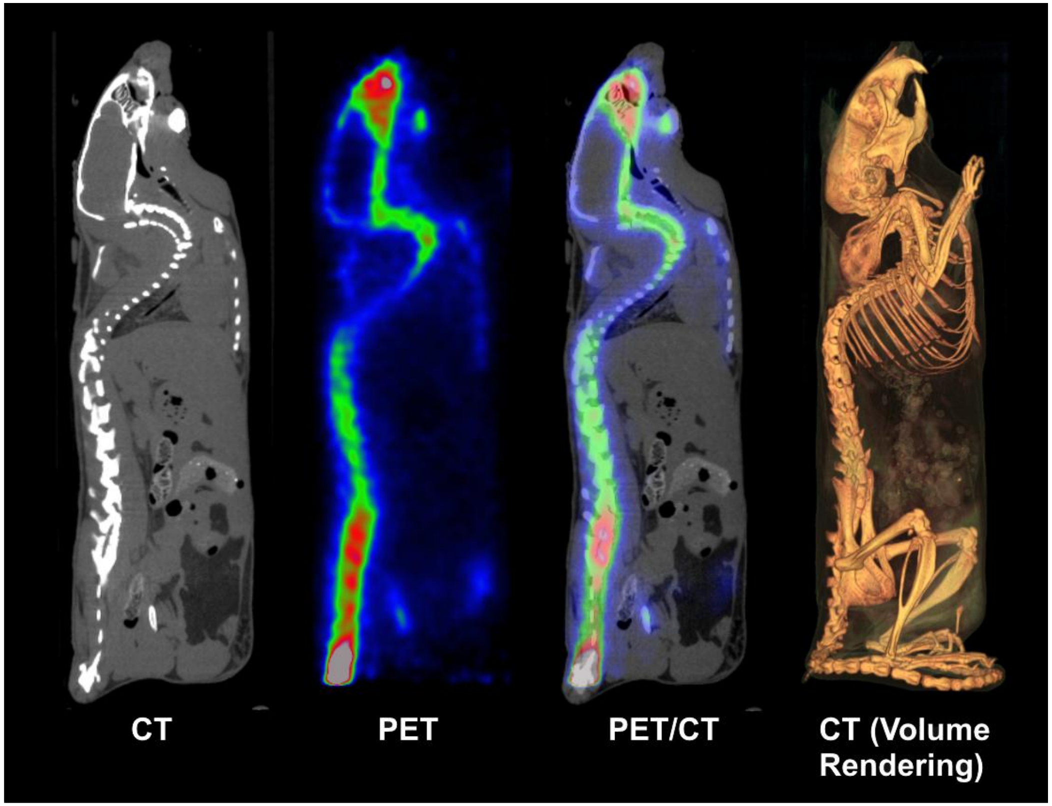
X-ray detector
- 1024 x 2048 pixels (48 μm each)
- 5 cm x 10 cm active area
- Maximum frame rate 2.7 fps
- 10lp/mm resolution

Xalt HR

X-ray source
- Fixed tungsten anode
- Maximum voltage: 50 kV
- Maximum power: 50 W
- Measured focus size: 20 μm FWHM
- Beam aperture: 22°

- Small animal CT with rotating gantry
- Variable geometry (spatial resolution / FOV size trade-off)
- Spatial resolution 30 μm
- Maximum diameter 8 cm

YAP-(S)PET + XaltHR



Hybrid imaging applications to a mouse

From left to right: CT image, PET image, fused image and volume rendering of the CT image

Technology transfer II: IRIS(raytest-Iviscan)

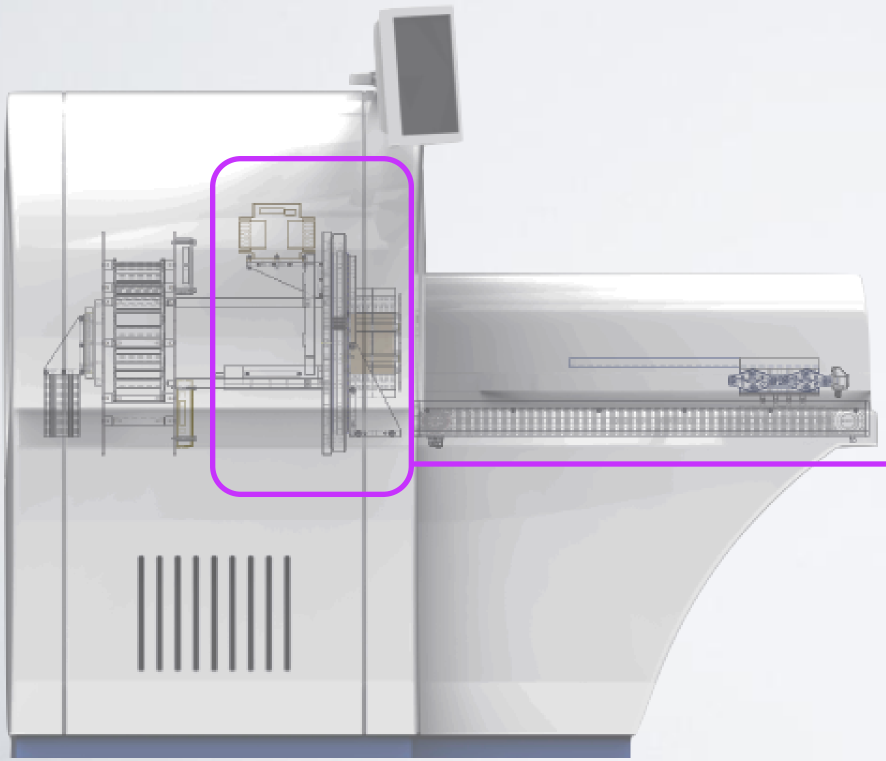
PET/CT SYSTEM FOR SMALL ANIMAL

- 16 PMT-based independent modules
- Octagonal geometry / Dual ring

PET

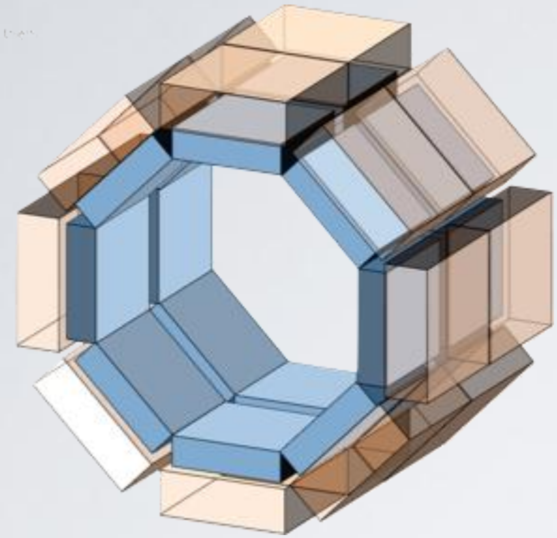
- Microfocus X-ray source
- CMOS + CsI flat panel detector

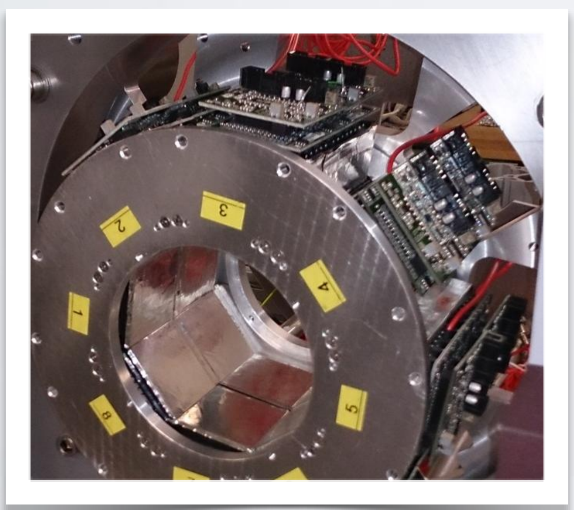
CT



PET and CT are attached to the same rotating gantry

IRIS PET System design





PET design and picture of the PET ring

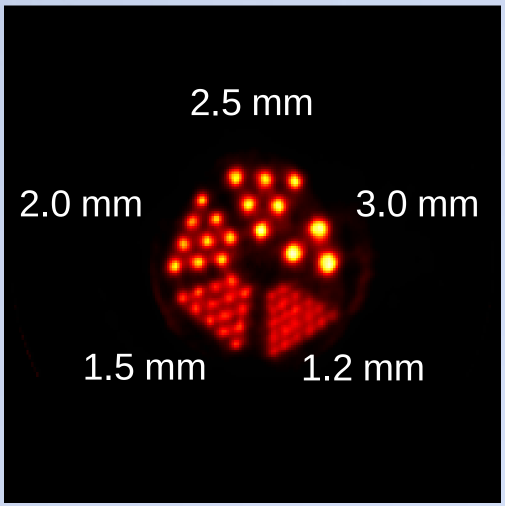
Detector module specifications	
Crystal material	LYSO:Ce
Crystal size (mm)	1.60 mm x 1.60 mm x 12 mm
Crystal pitch (mm)	1.68 mm
Crystals per module	27 x 26
Photodetector	MA-PMT 64 ch. (resistive chain readout)
System specifications	
No. of modules	16
No. of rings	2
Bore size (mm)	100 mm
FOV size (mm)	80 mm (T) x 95 mm (A)
Other features	
PET Detector rotation	

SOme imageS - PET

Rotating acq.

Derenzo phantom image

- 2 MBq of ^{18}F
- 20 min. scan time

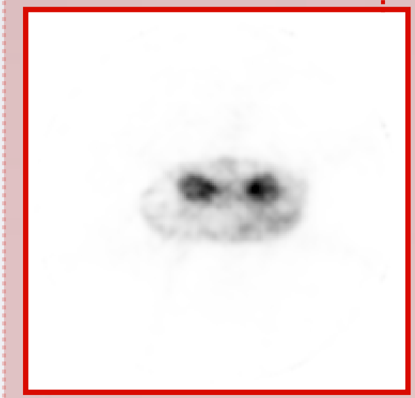


ML-EM reconstruction 70 it.

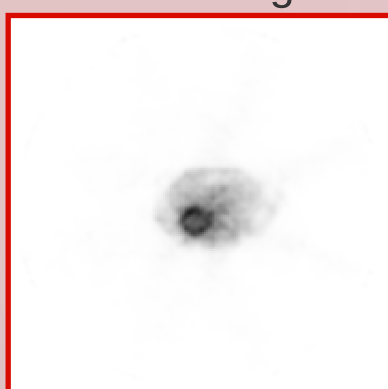
Static acq.

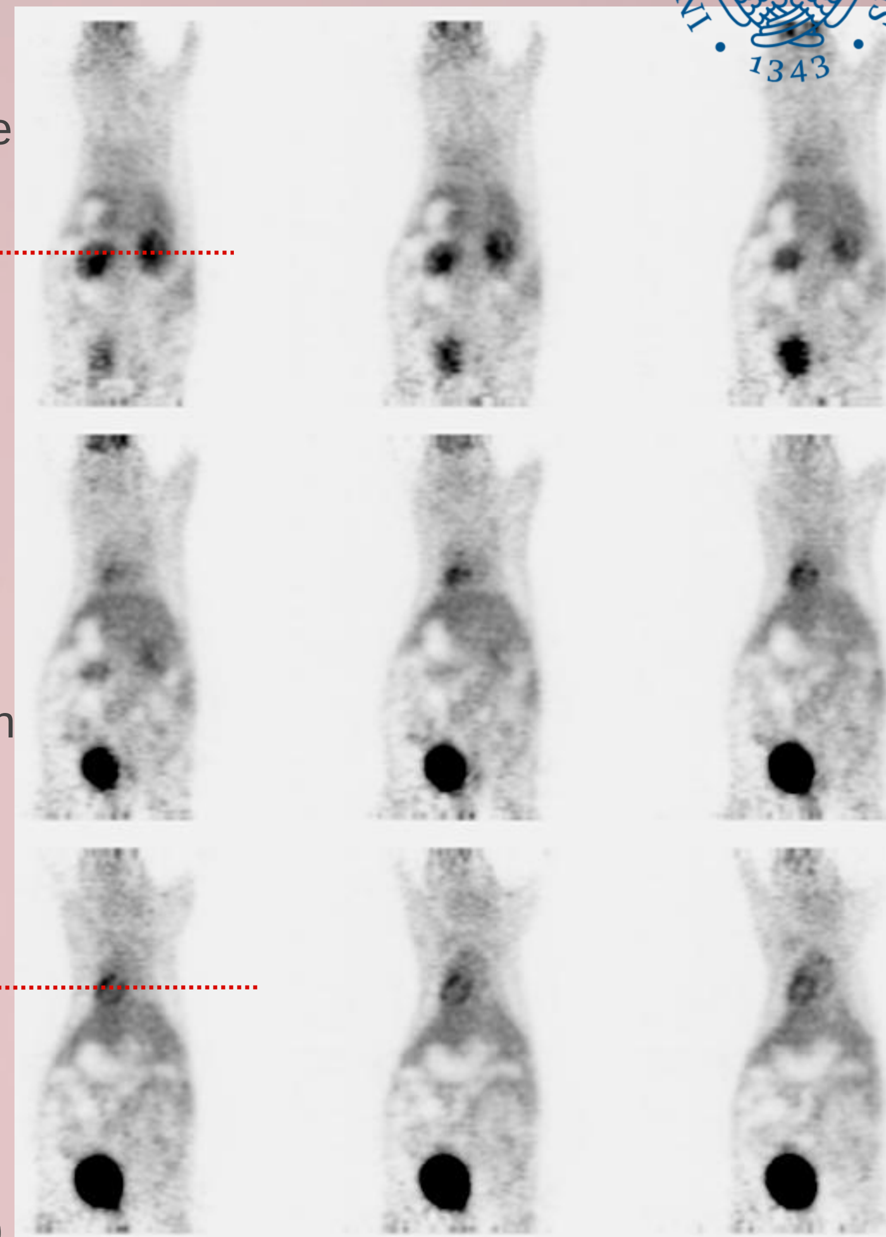
In-vivo Mouse image

- 2 MBq of ^{18}F-XXX
- 15 min. scan time



ML-EM reconstruction 70 it. with 1mm (σ) post smoothing





All images displayed in a single slice with: 0.420 x 0.420 x 0.855 mm^3 voxel size

IRIS PET/CT performance

IRIS PET/CT

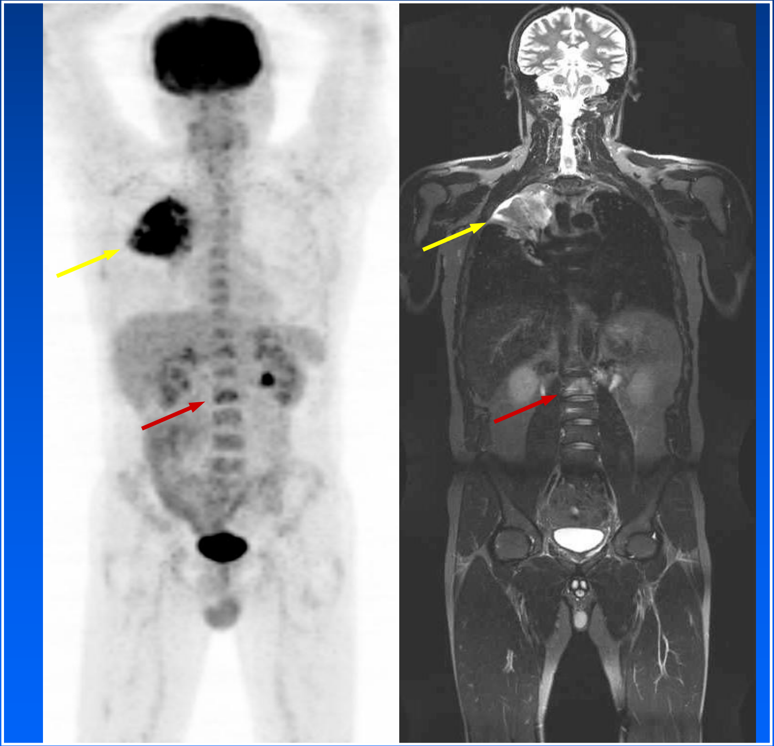
- IRIS PET/CT shows optimal performance for pre-clinical imaging (1.5 mm^3 volume resolution at CFOV)
- Maximum absolute sensitivity is among the highest in the market 250-750 keV: 9.8%)
- The unique rotating detector feature offers higher quality images with very high uniformity (4.7% @ 50 it. ML-EM)
- Rotating acquisitions are well suited, e.g., for biodistribution (non-dynamic) studies.

Hybrid Systems
PET/MR

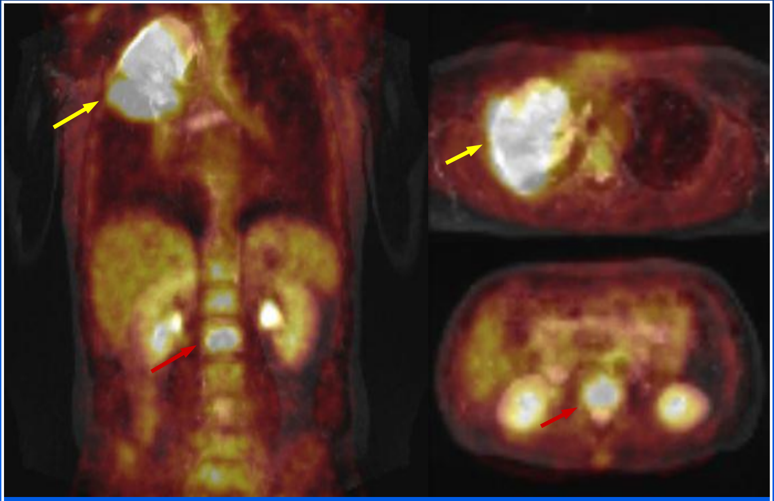
MR/PET:“one-stop-shop”

New whole-body imaging procedures allow comprehensive imaging examinations

Fused MRI/PET facilitates accurate registration of morphological and molecular aspects of diseases



Coronal overview of 18F-FDG PET and MRI (T2- weighted Turbo-STIR)



Pulmonary and osseous (arrow, red) metastatic disease of a non-small cell lung cancer (arrow, yellow)

Coronal and transversal MRI/PET fusion images

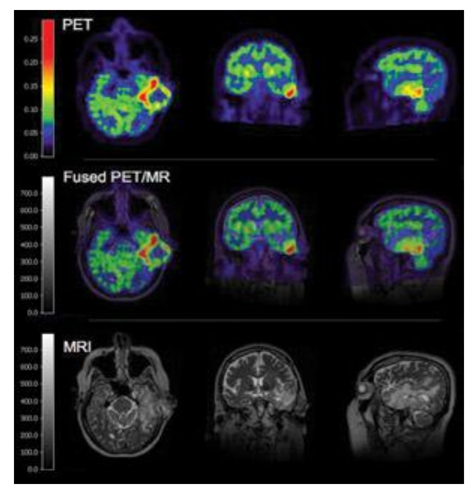
Courtesy of Dr. Gaa, TU Munich

Why PET/MRI?

Nowadays there are systems where PET and MRI are performed separately in time with distinct machines:

- Two images to be merged together
- Movements of the patient on the couch
- Data corruption from image fusion techniques

Philips Ingenuity TF PET/MR Combo

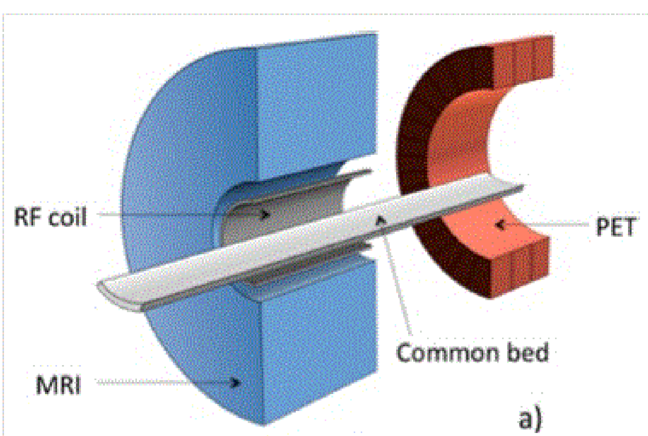


PET and MRI image fusion

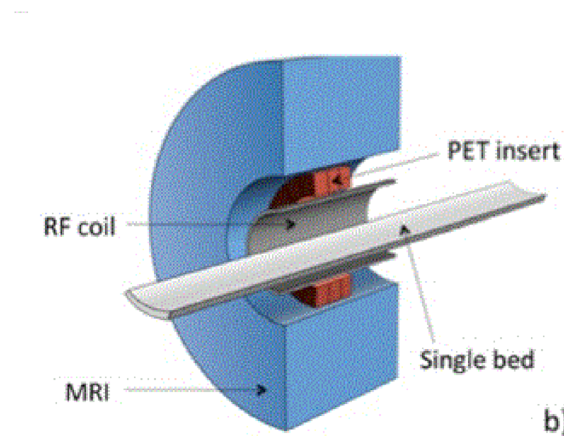
Why Combined PET/MRI?

Hybrid PET/MRI systems provide functional and morphological information *at the same time*:

- No image fusion required
- Space and costs saving
- Better soft tissue contrast
- Lower radiation doses

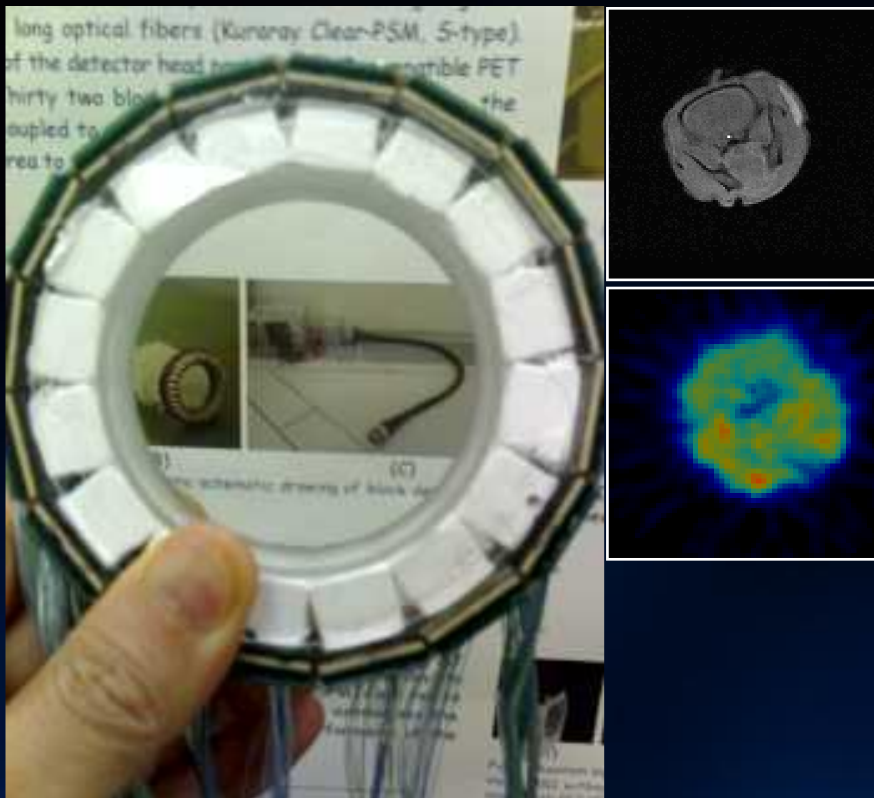


Separated PET and MRI rings

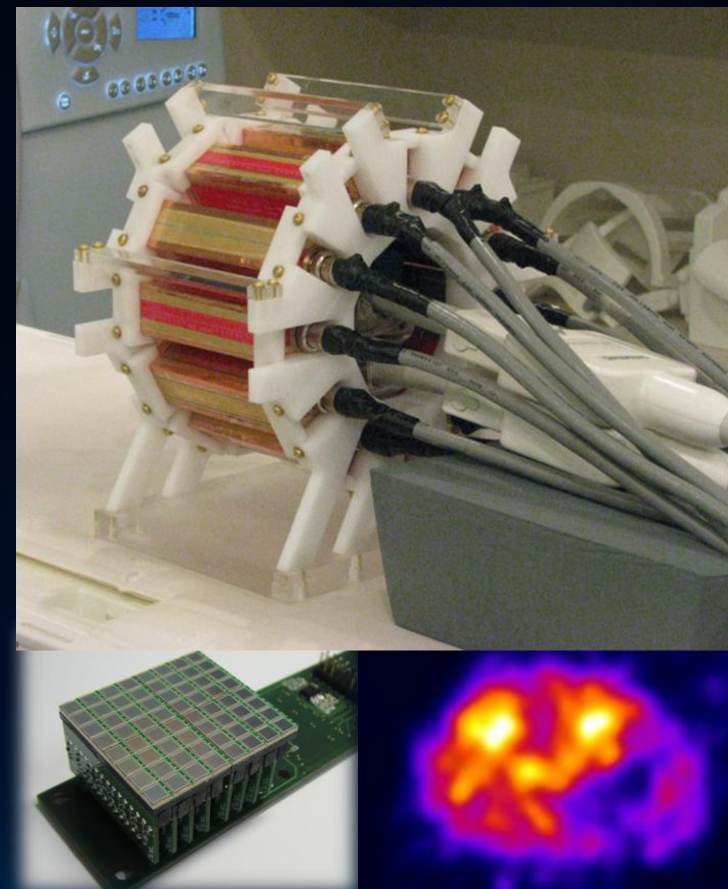


Hybrid PET/MRI scanner

SiPM-Based PET/MRI

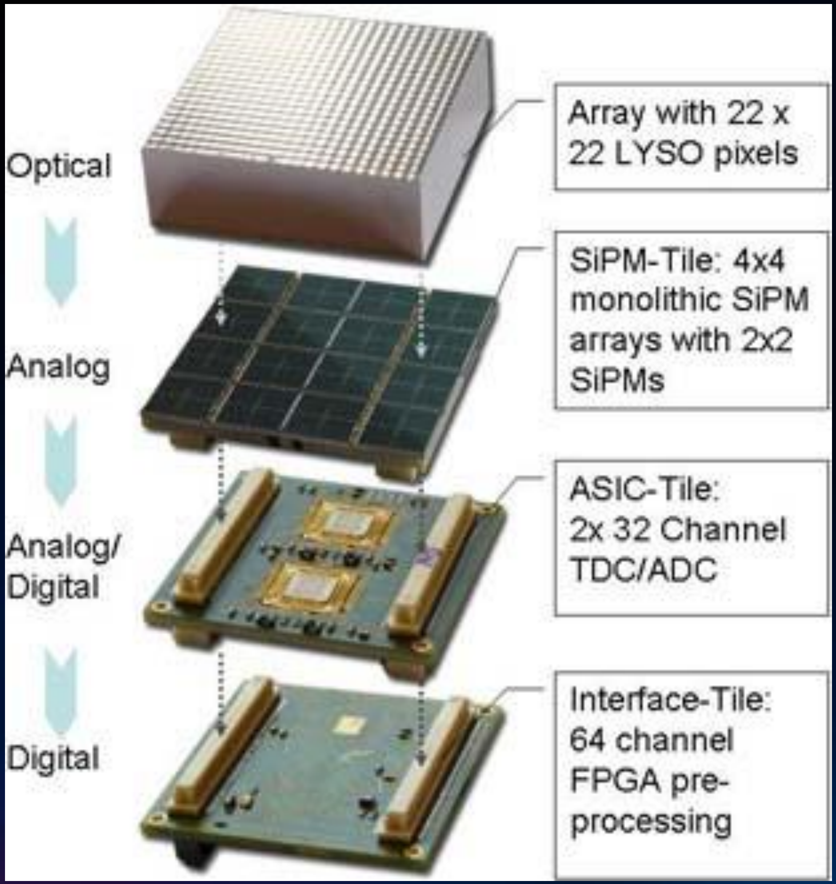


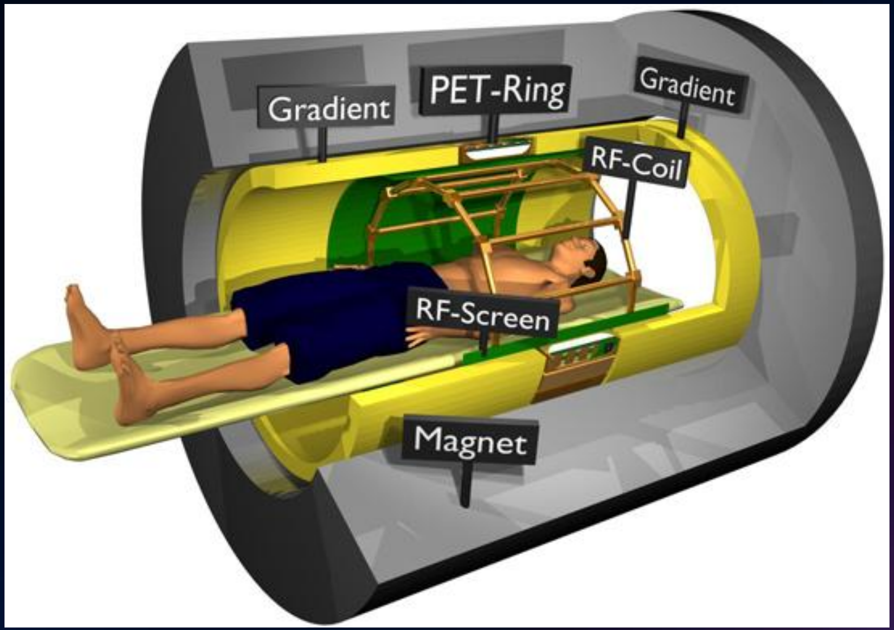
Courtesy of Seiichi Yamamoto
Kobe University



Courtesy of Jae Sung Lee,
Seoul National University

Human TOF PET/MRI based on SiPMs

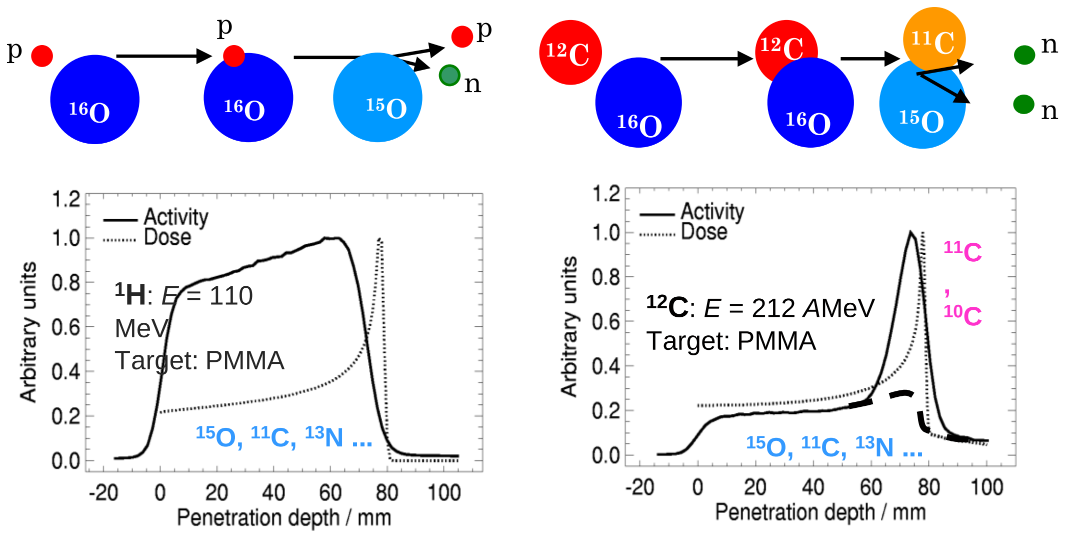




HYPERimage consortium: http://www.hybrid-pet-mr.eu/

PET in HADRONTHERAPY

In-beam PET monitoring



A possible method for the control of the geometrical accuracy of the treatment (TPS) is PET imaging

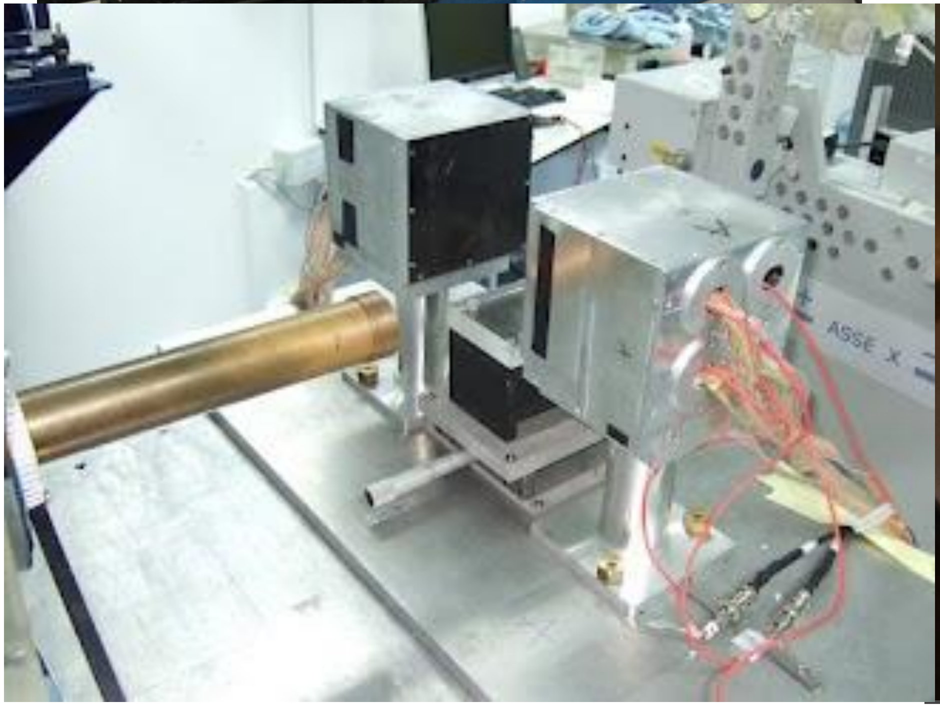
- Nuclear inelastic reactions between the hadron beam and nuclei in tissue
- Small amounts of β^+ emitting isotopes are produced with short half-lives like
  - ^{11}C (20.3 min),
  - ^{13}N (9.97 min),
  - ^{15}0 (2.03 min).

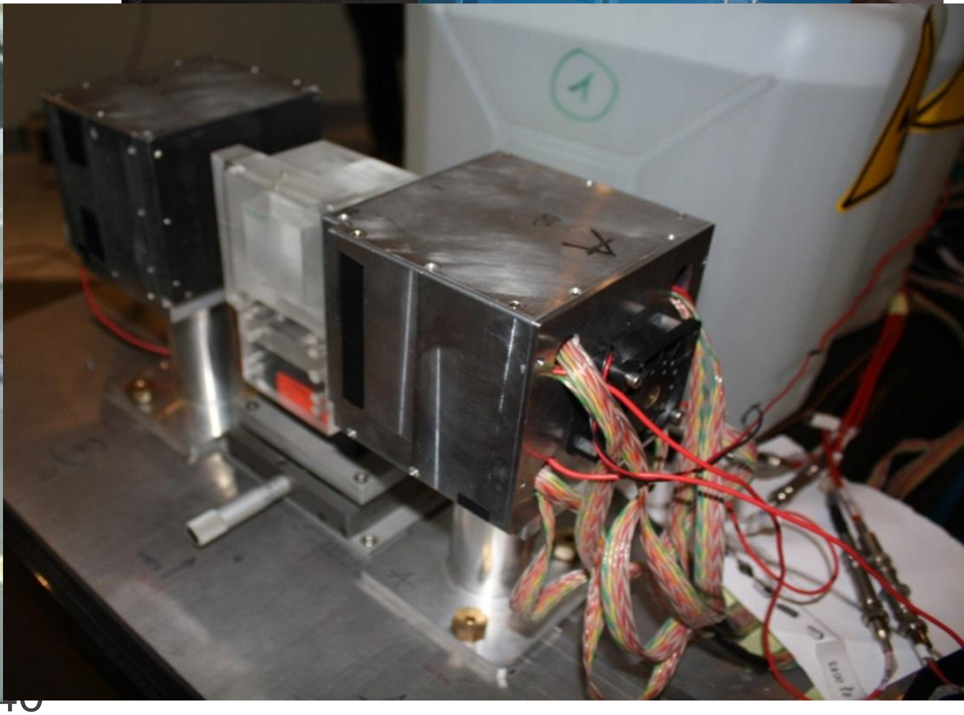
In-beam/in-room dedicated instruments are necessary to:
- Avoid patient re-positioning
- Avoid data loss of very short living isotopes

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

Experimental setups @

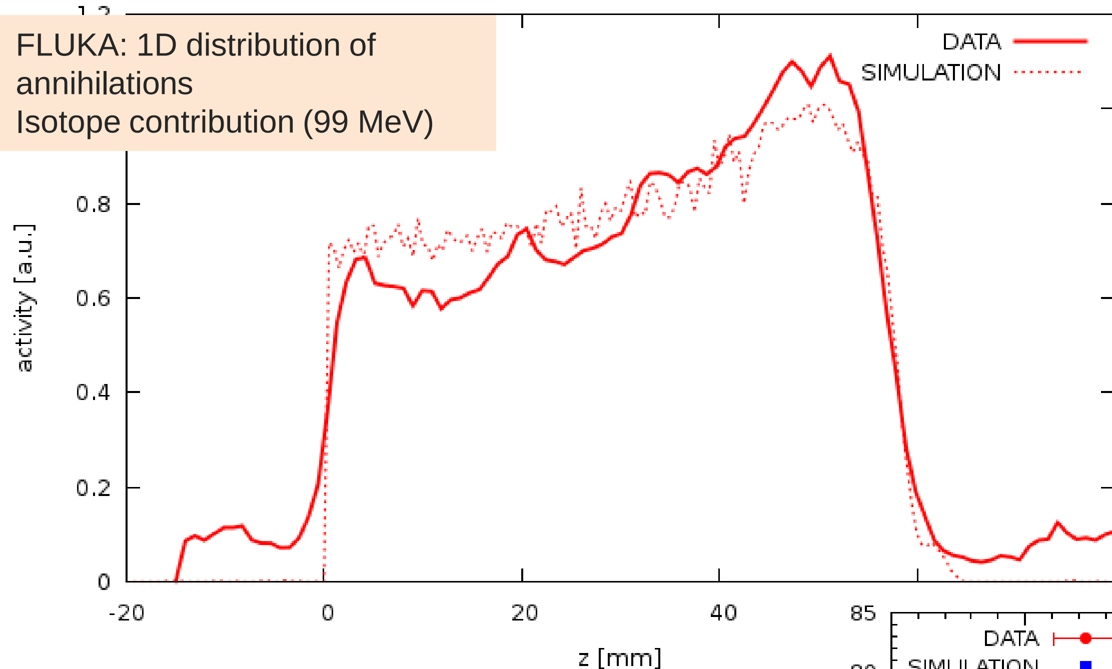
CATANA (62 Mev p Cyclotron) and **CNAO** (p and 12-C synchrotron)



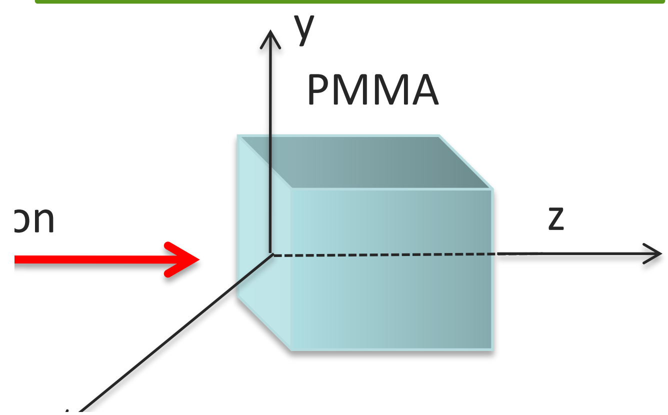


Simulation vs Experiment

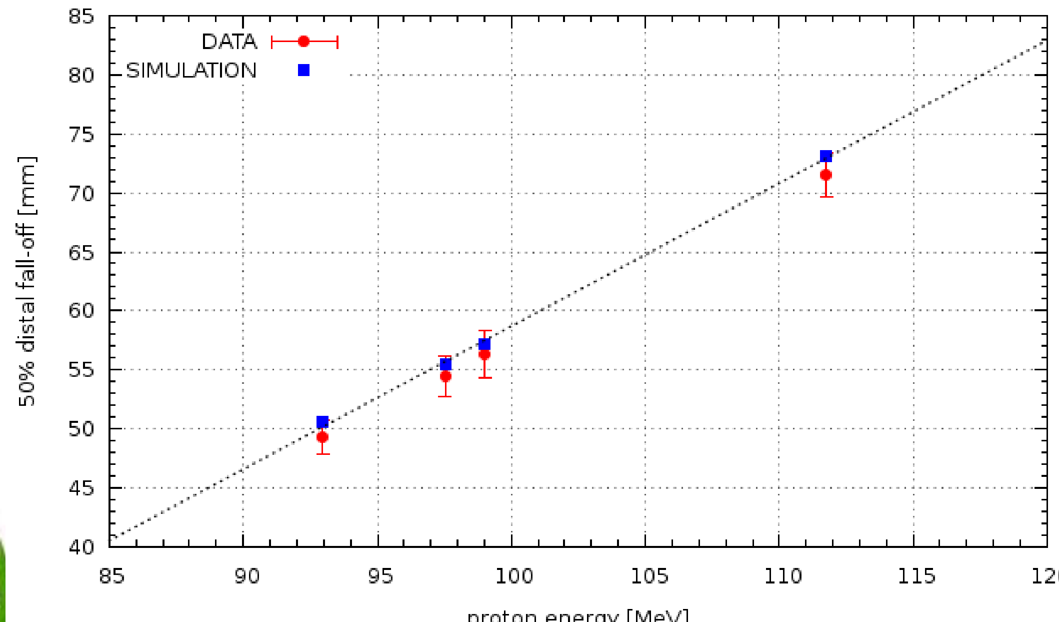
FLUKA: 1D distribution of annihilations
Isotope contribution (99 MeV)

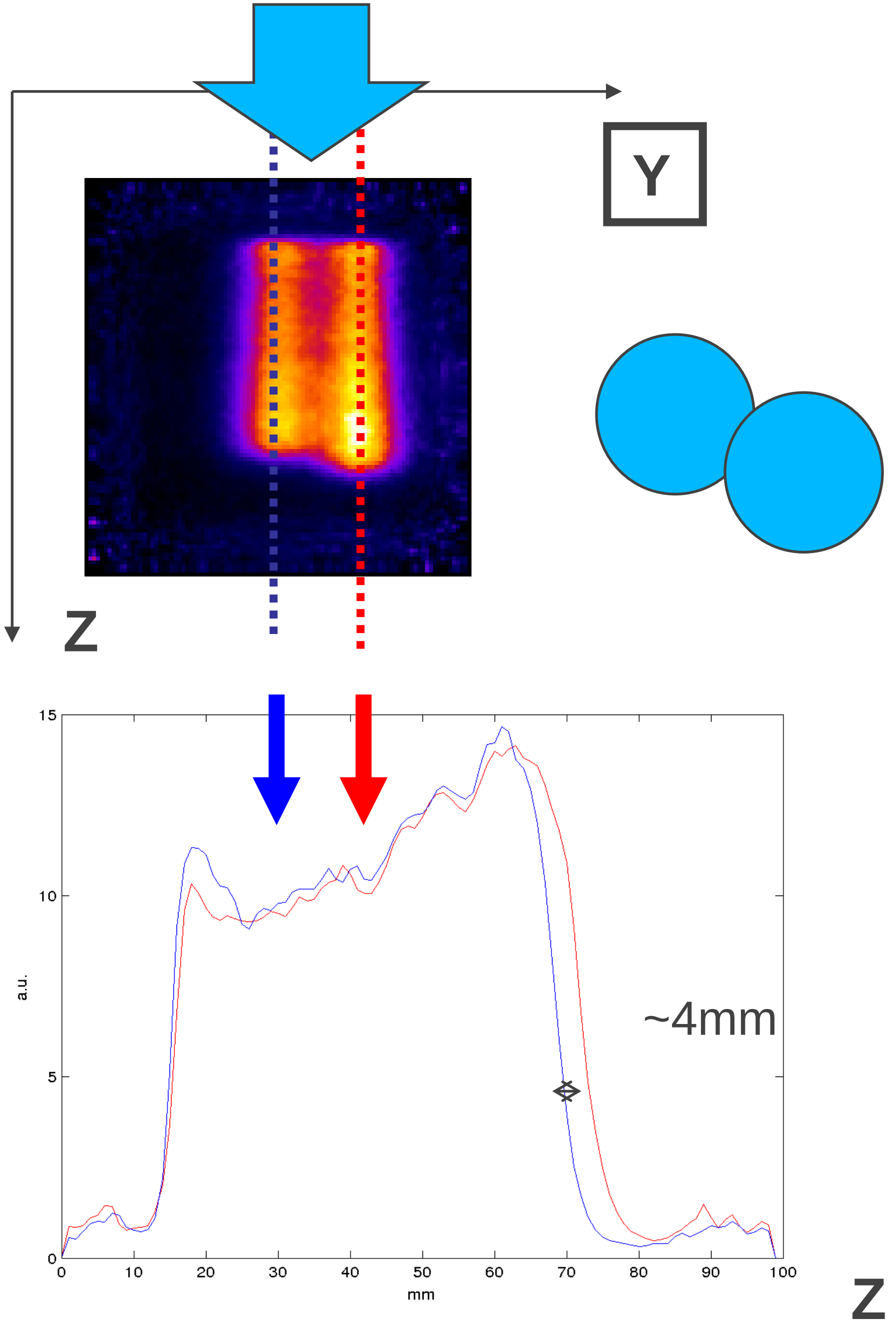


CNAO: proton beam 99 MeV on PMMA



Comparison of the position of the 50% fall-off between FLUKA simulation and exp data for 93, 97.5, 99, and 112 MeV protons (1mm agreement)
The error bar is the σ of the fit.





CNAO data at 95.34 and 98.32 MeV protons

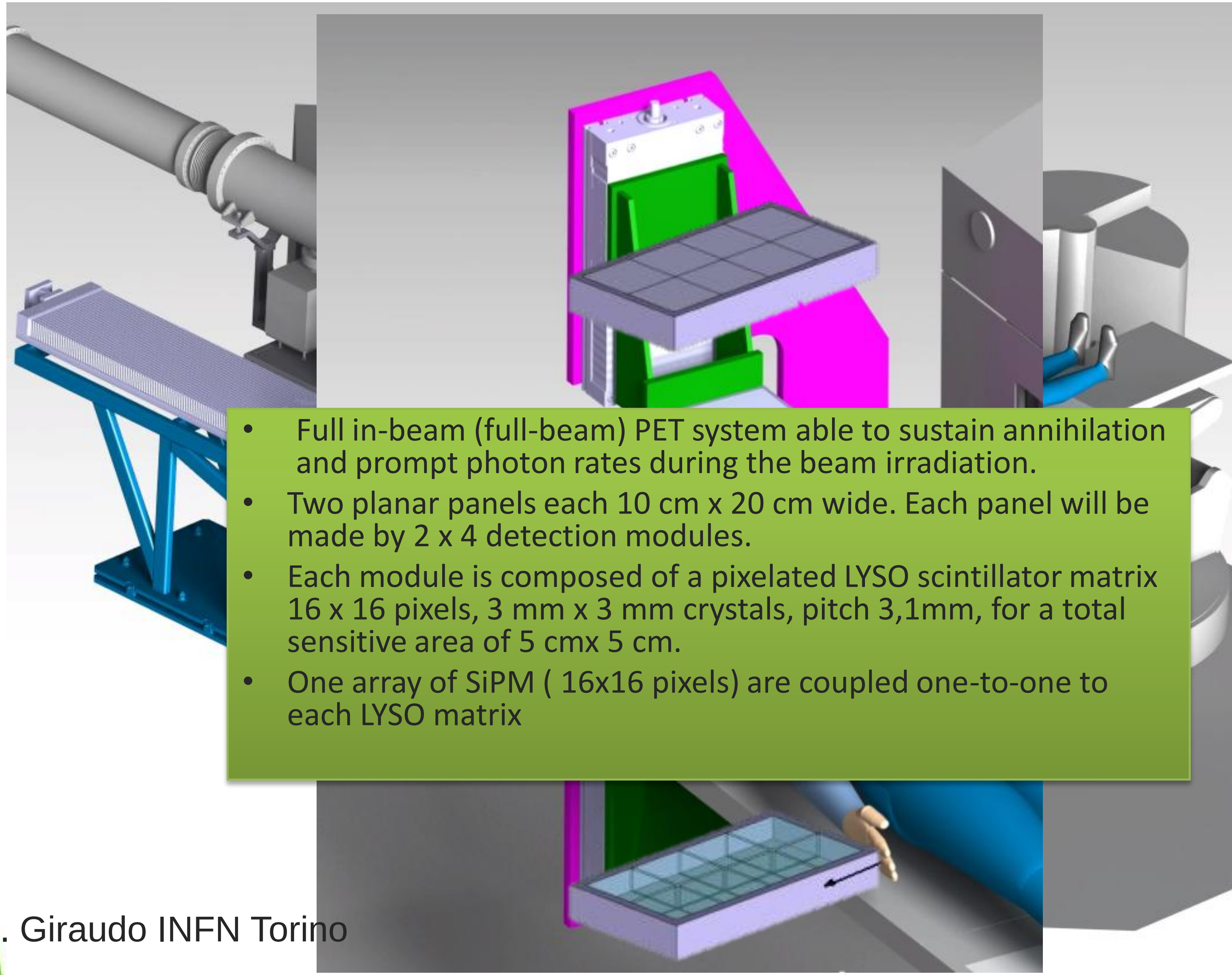
(beam-off data Δt ~ 14')

$$f(x) = 1.22 \cdot x - 63.3$$

$$f(98.32) - f(95.34) = 3.7mm$$

INSIDE Project: INnovative Solutions for In-beam DosimEtry in Hadrontherapy

- PRIN MIUR 2010-2011 - 2010P98A75 - INSIDE
- Coordinator: Alberto del Guerra, University of Pisa
- Duration 3 years from February 1,2013
- Funds from MIUR: about 1M€
- 5 Research Units
  - Universita' di Pisa (A. Del Guerra)
  - Bari Politecnico (F. Corsi)
  - Universita' di Roma La Sapienza (V. Patera)
  - Universita' di Torino (C. Peroni)
  - INFN (G. Battistoni)
- 40 Researchers

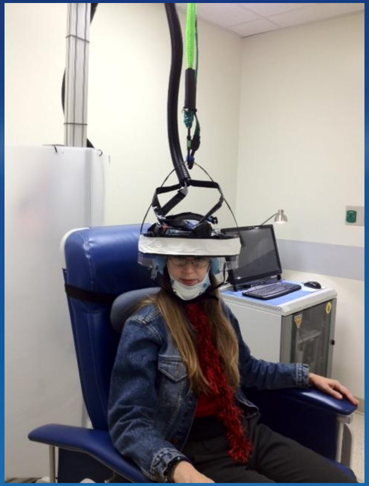


- Full in-beam (full-beam) PET system able to sustain annihilation and prompt photon rates during the beam irradiation.
- Two planar panels each 10 cm x 20 cm wide. Each panel will be made by 2 x 4 detection modules.
- Each module is composed of a pixelated LYSO scintillator matrix 16 x 16 pixels, 3 mm x 3 mm crystals, pitch 3,1mm, for a total sensitive area of 5 cmx 5 cm.
- One array of SiPM (16x16 pixels) are coupled one-to-one to each LYSO matrix

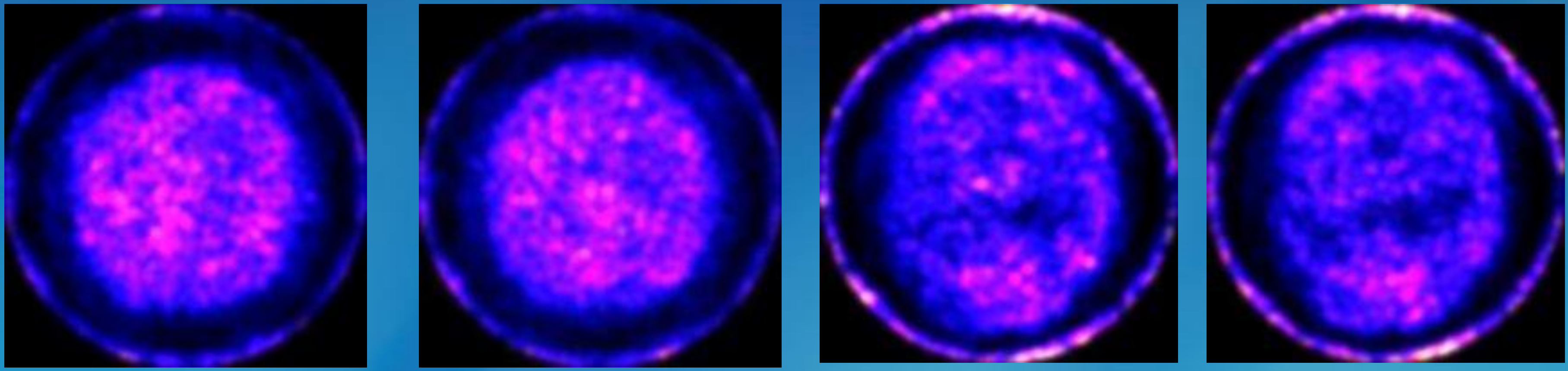
BRAIN PET

CENTER FOR ADVANCED IMAGING
AT WEST VIRGINIA UNIVERSITY

Jefferson Lab | AiT Instruments | AGILE TECHNOLOGIES



The Helmet PET portable PET ring imaging system is able to image patients in the upright position. This enables for example obtaining molecular brain images of the stroke patients to assess treatment and recovery of brain function. In addition, it is a useful tool in basic research in regards to the relationship between motor tasks and brain metabolism. The suspended imager follows the limited head movements of the sitting patient.



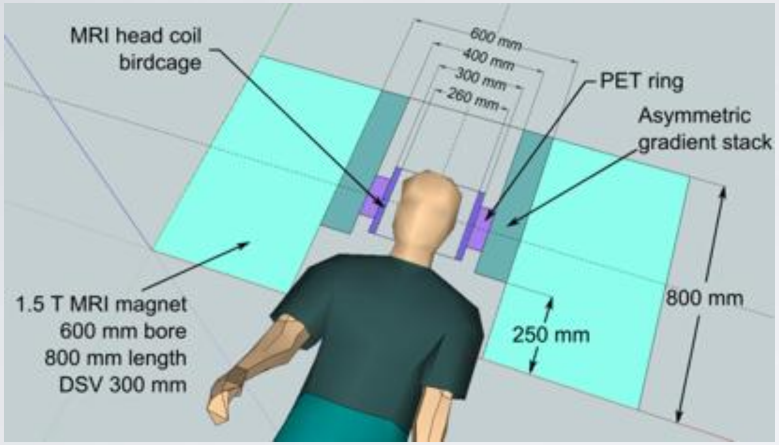
Preliminary first patient images (10/25/12). Imaging of the ~4cm brain section performed ~4 hours post-injection of 12 mCi of F18-FDG. 600 sec data collection. Shown four selected reconstructed 1mm image slices, two neighboring at the top of the brain slice (left) and two neighboring at the lower part of the brain slice (at right).

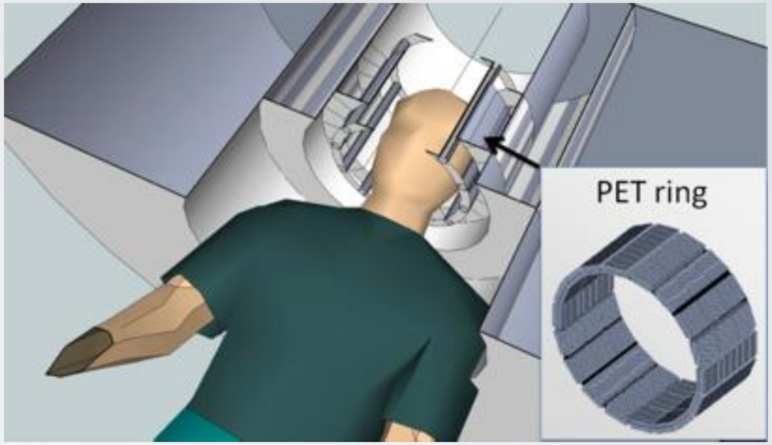
TRIMAGE

“An optimised trimodality (PET/MR/EEG) imaging tool for schizophrenia”

FP7- funded project under Health (starting 1 December 2013- 4 years)
Coordinator: A.Del Guerra (Pisa)

A closer LOOK at the instrument





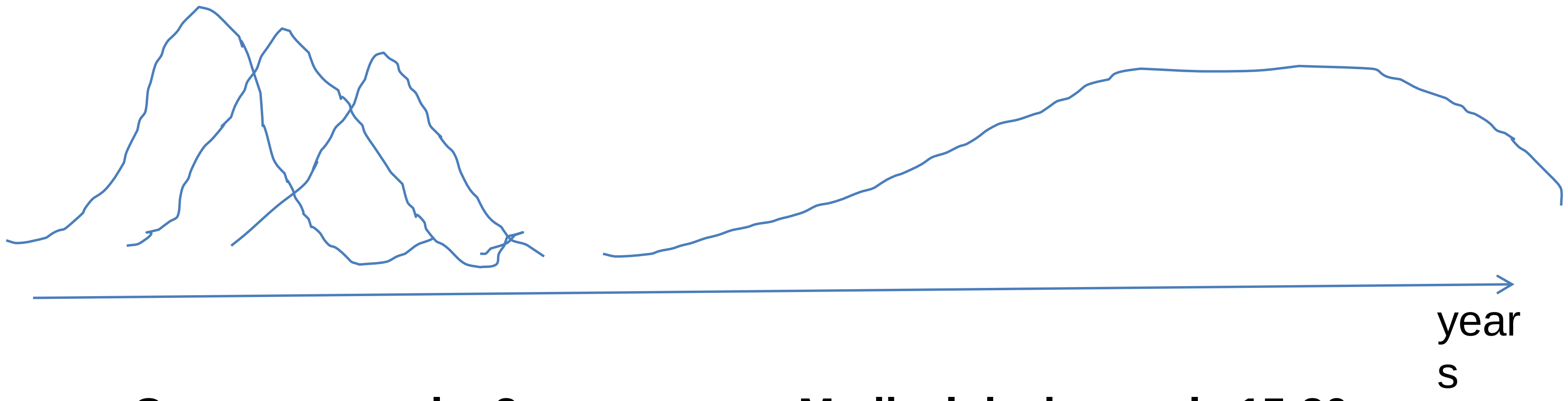
Dimensional outline (left) and artistic view (right) of the dedicated brain PET/MR/EEG system (the EEG cap is not shown).

CRITICITY MR
-800 mm bore
- Asymmetric gradient
-low field 1.5 T

CRITICITY PET
- sp res 2mm (DOI)
- high efficiency
- axial FOV

low-cost

CONCLUSIONS



Consumer cycle: 3 y **Medical device cycle 15-20 y**

Take home message:

- TT in the medical field needs long term investment
- Industry can withdraw half-way through, if not profitable,e.g. Siemens for proton therapy

Ref: Freely adapted from the keynote talk by Dr. Jaemoon Jo (SamsungSenior Vice-President) at NSS_MIC_2013, Seoul, 30 Oct 2013

Take Home Message

- *MULTIMODALITY is the future:*
  - *PET/CT*
  - *PET/MR*
  - *PET/OPT,Cherenkov*
  - *and more…*
- *PET organ/application specific is the future:*
  - *Brain*
  - *Breast*
  - *Prostate*
  - *Hadrontherapy*
  - *and more…*

THANK YOU !

Acknowledgments:
- INFN (4DMPET) [2010-2013]
- Envision (FP7 project) [2010-2014]
- Inside (PRIN 2010) [2013-2015]
- TRIMAGE (FP7 project) [2013-2017]
- ... and ...