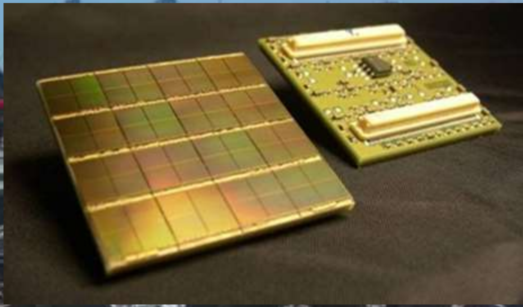
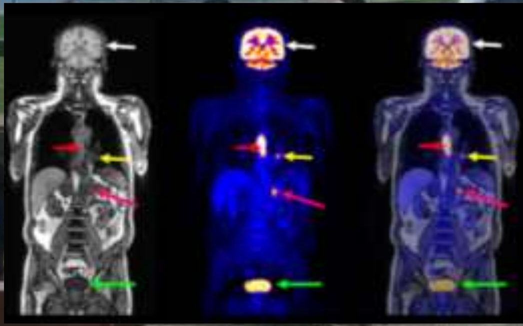
Current Challenges and Opportunities in Positron Emission Tomography

Paul Marsden
King’s College London



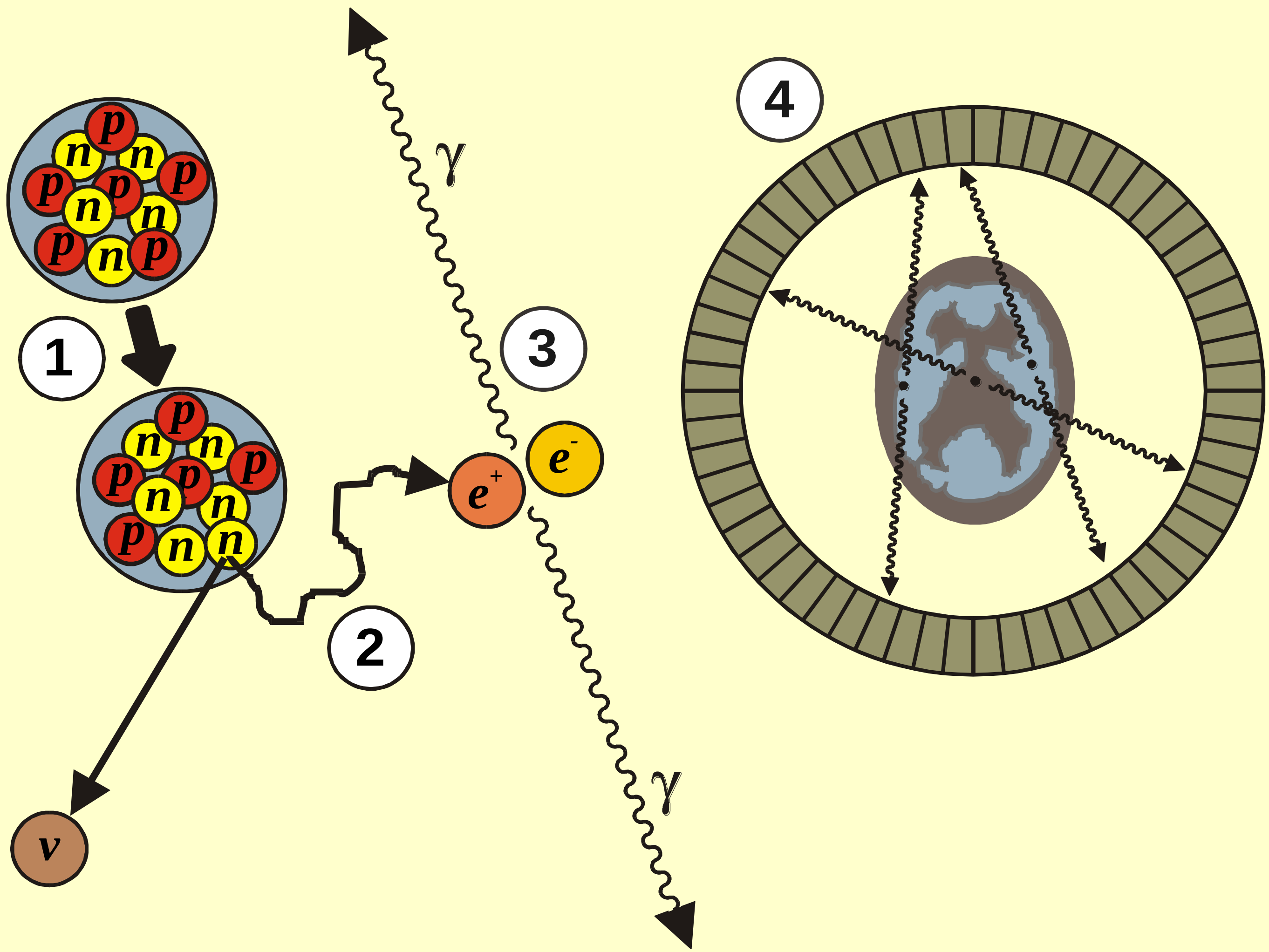


STFC Particle Physics Department
Rutherford Appleton Laboratory - 3 Sept 2014

Current Challenges and Opportunities in Positron Emission Tomography

- *Basic principles and applications*
- *Limits to performance*
- *Current developments*
- *Challenges and opportunities*

Annihilation coincidence detection

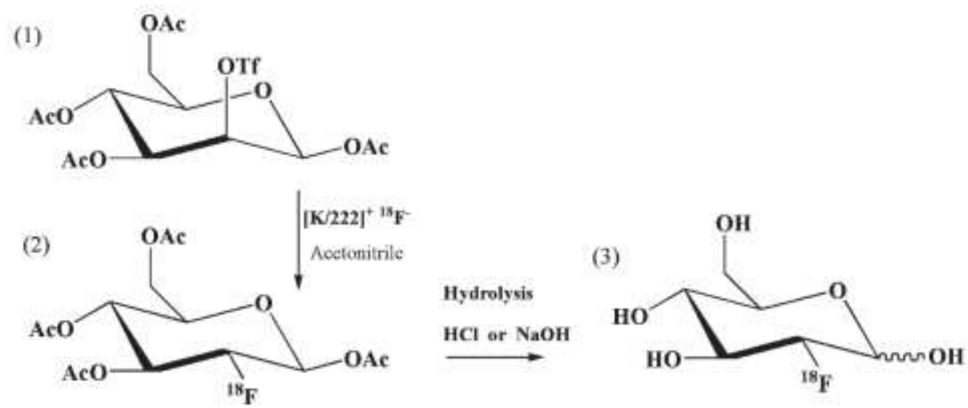


Detection of pmolar concentrations of tracer

Cyclotron

Hot cells

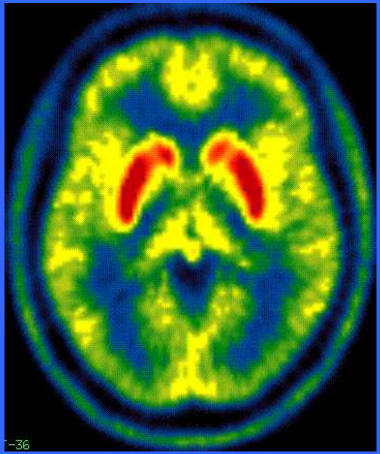
Synthesis units



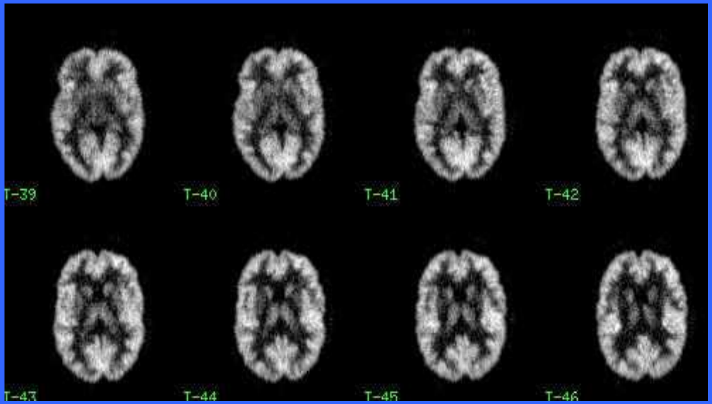
Chemistry

Specificity of PET radiotracers

^{18}F-DOPA

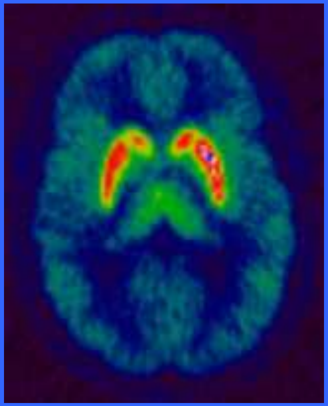


^{11}C-MDL 100907

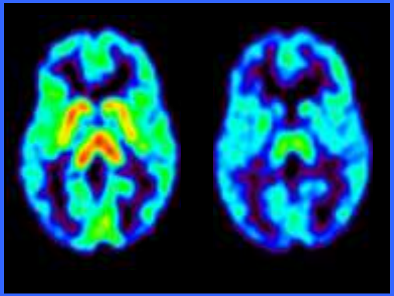


^{11}C-Raclopride

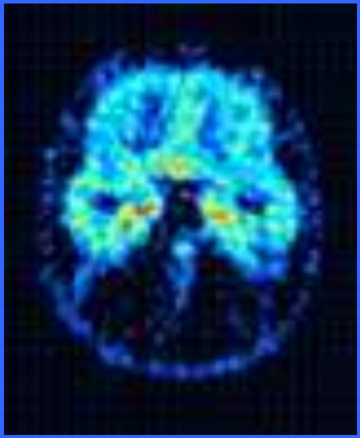
^{11}C-FLB 457



^{11}C-DASB

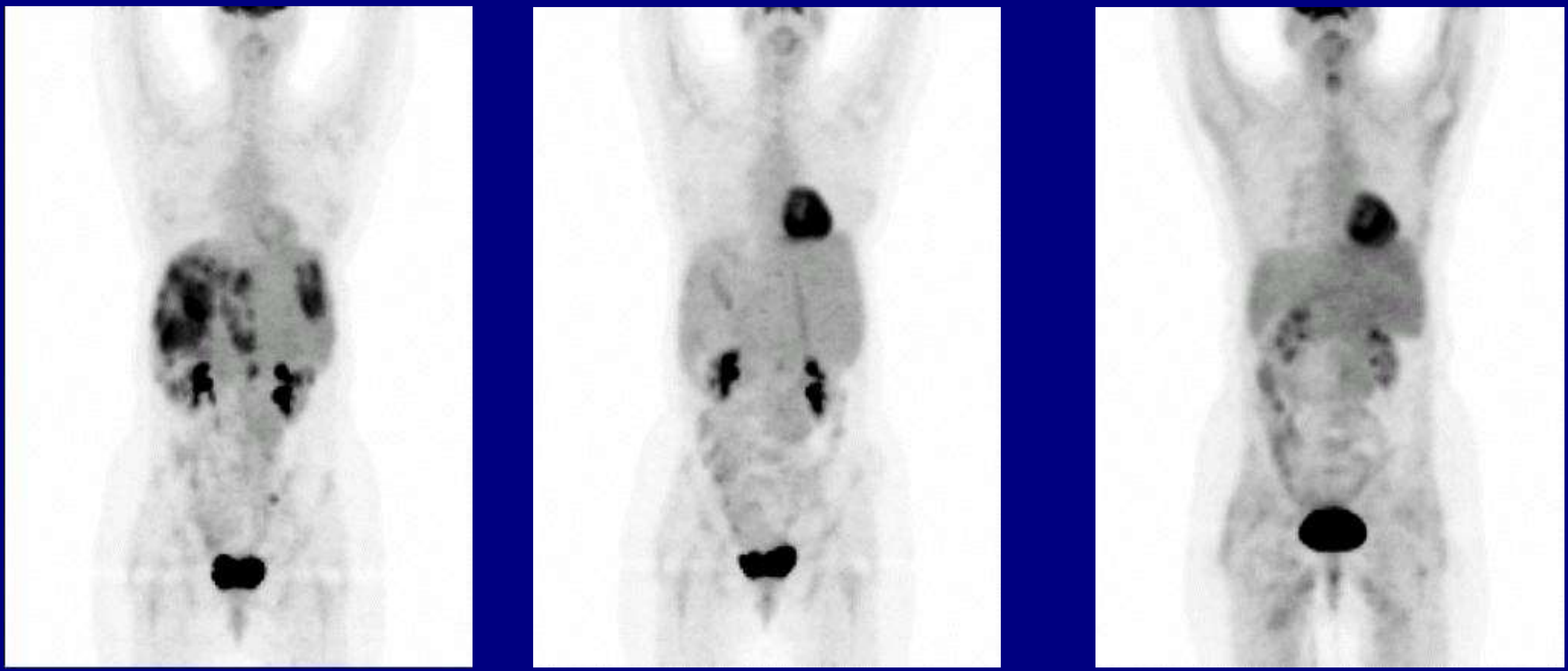


^{11}C-WAY 100635



Paul Grasby, MRC Clinical Sciences Centre

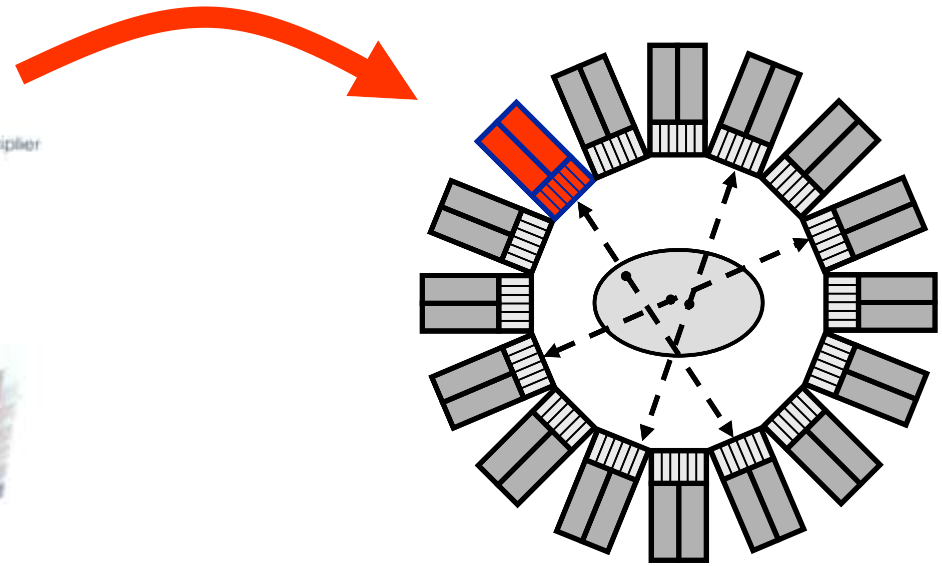
FDG-PET demonstrates response to Gleevec (tyrosine kinase inhibitor) in gastrointestinal stromal tumor (GIST)



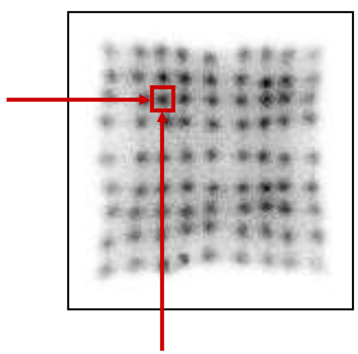
Baseline | Day 1 | 3 years

Van den Abbeele et al - Dana-Farber Cancer Institute

Standard scanner configuration

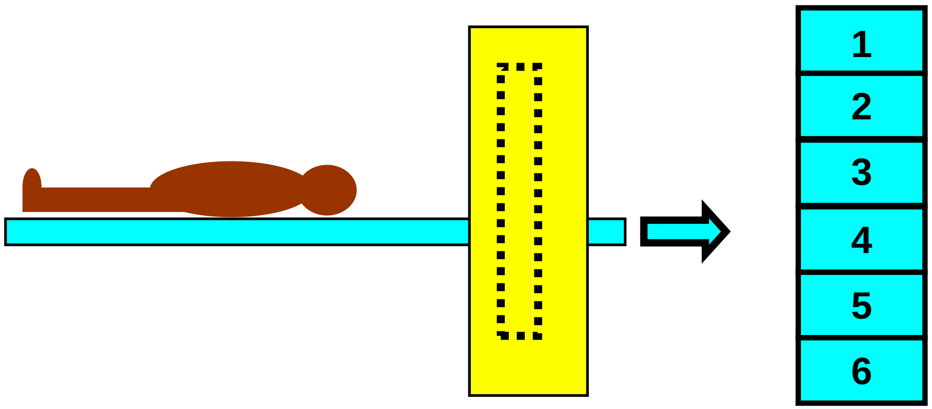


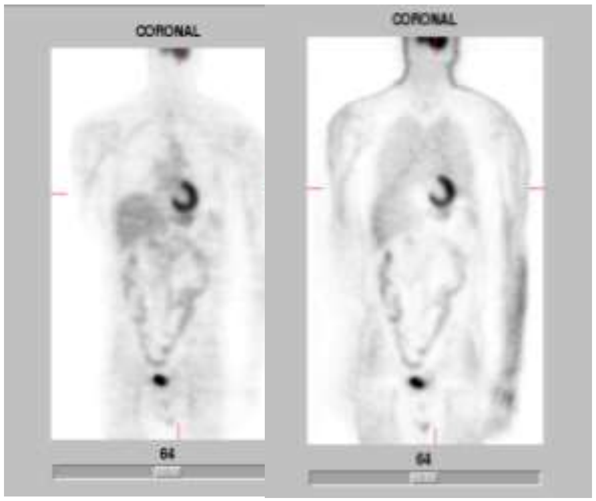
$$Y = \frac{A+C}{A+B+C+D}$$



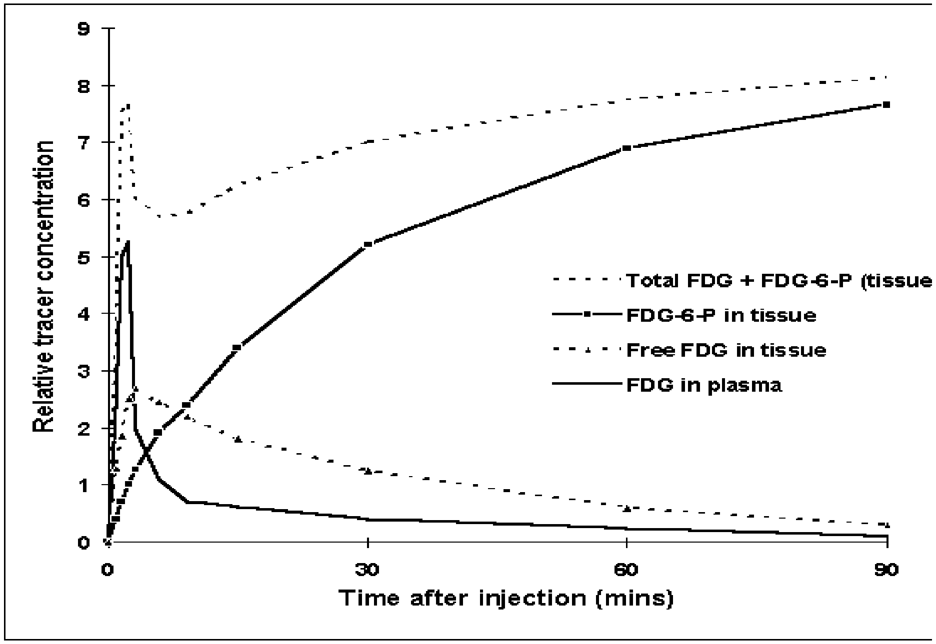
$$X = \frac{A+B}{A+B+C+D}$$

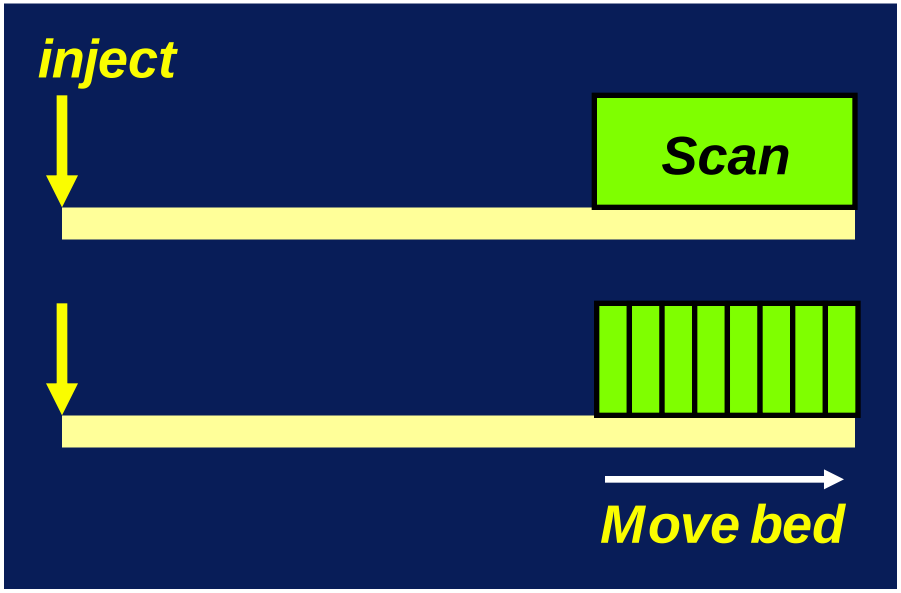
Whole body protocol



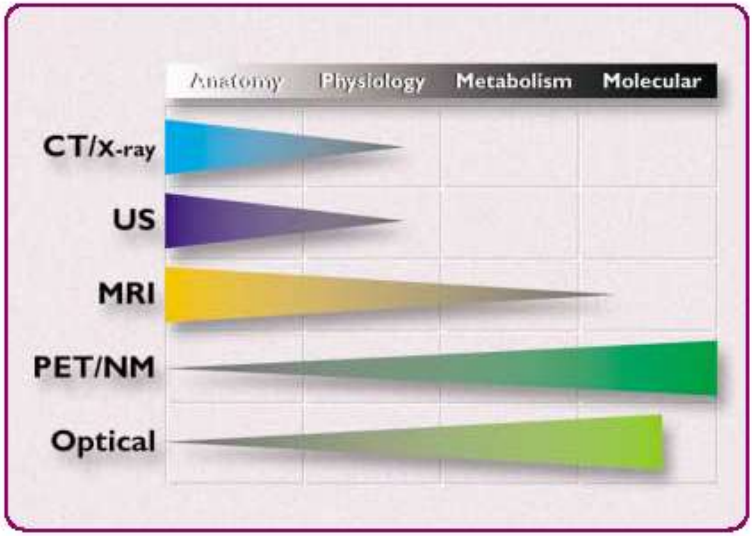


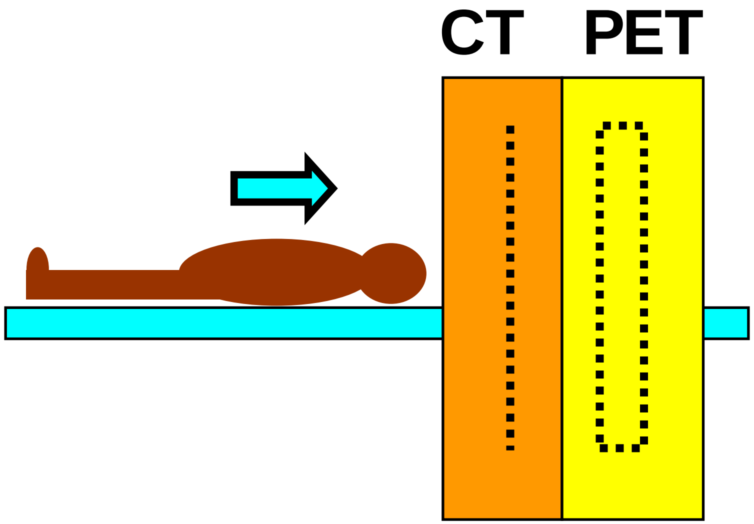
AC No AC

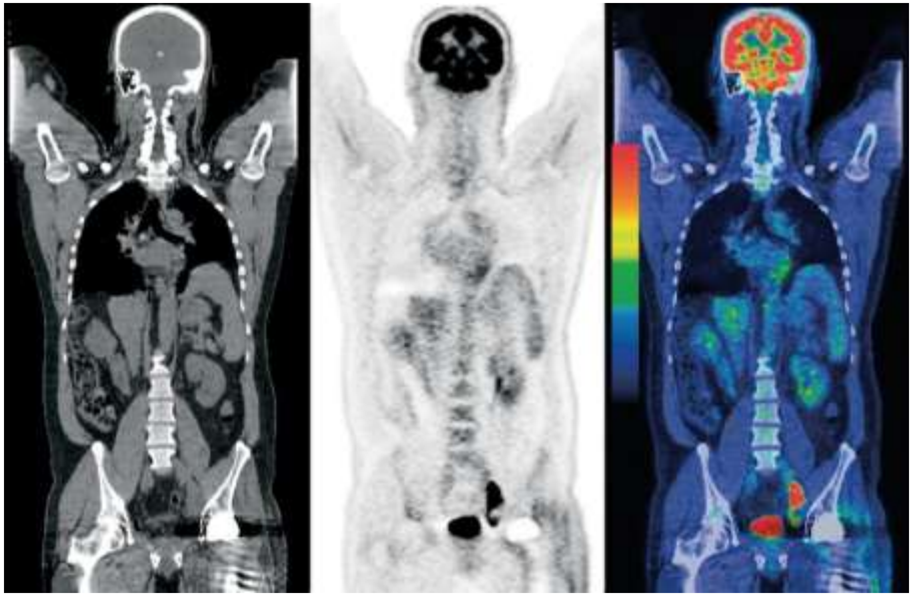




Multimodality: combined PET-CT systems







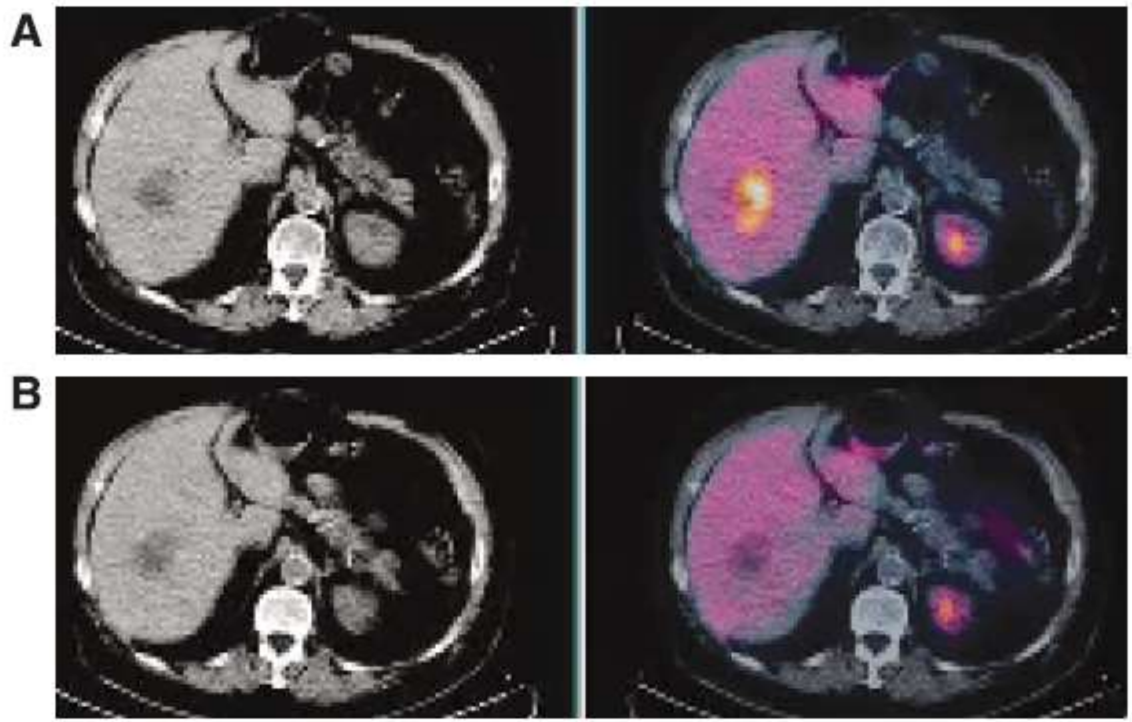
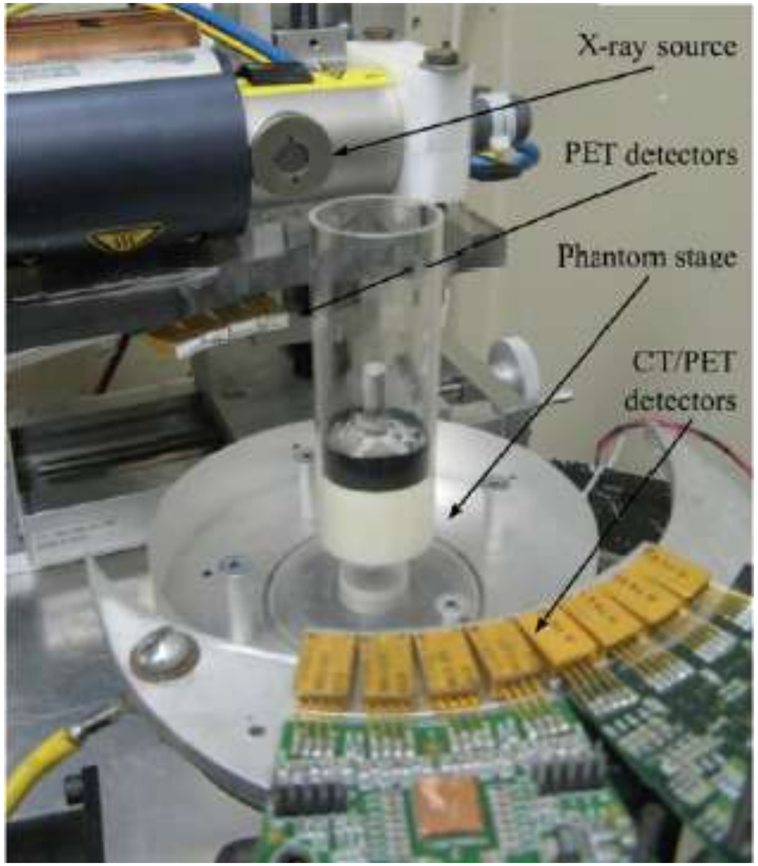
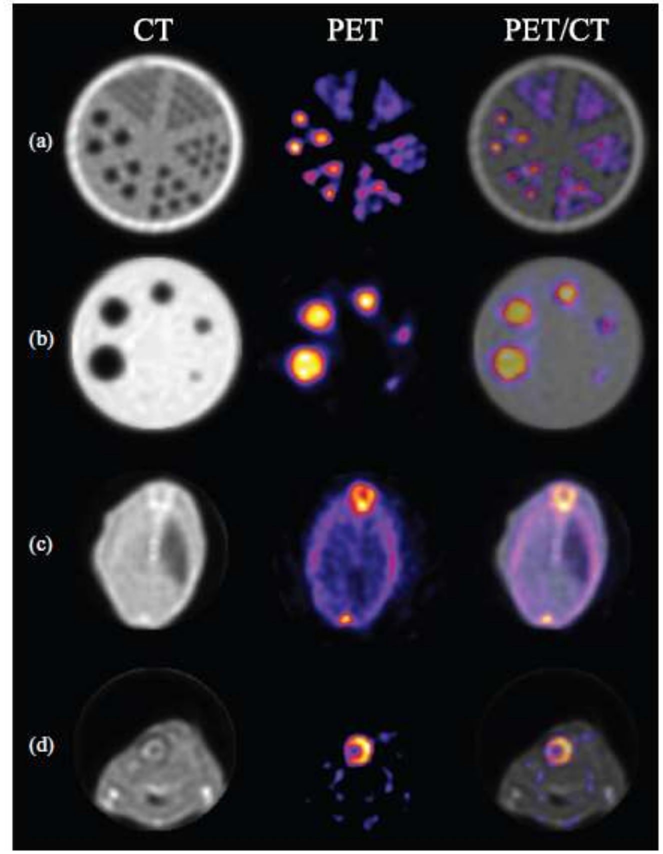


Figure 1 A liver metastasis from a gastric GIST before (**A**) and 1 week after (**B**) commencing imatinib therapy. FDG PET/CT scans, unenhanced CT (left), fused FDG PET and CT (right). Although there has been no morphological change in the metastasis, the abnormal baseline metabolic activity (colour scale) has rapidly resolved indicating sensitivity to the drug. The SUV fell from 5.0 to 1.8.

Combined PET/CT imaging – very different detector technologies





'LabPET' APD small animal PET system

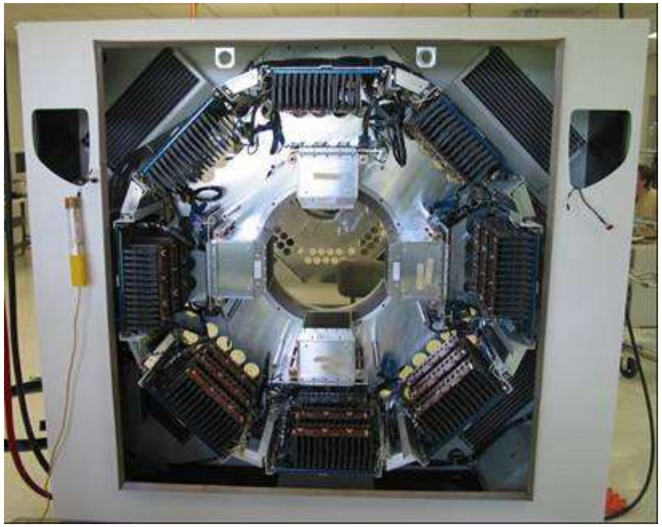
PET – pulse mode/poor spatial resolution (1mm here)

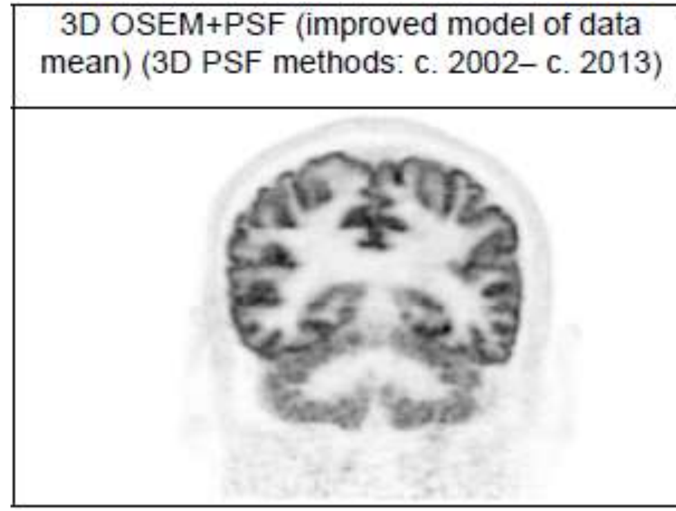
CT – 50keV/current mode/high spatial resolution (typically 100um)

- photon counting mode CT acquisition (energy discrimination..)
- But..little motivation for human systems as imaging times are so different

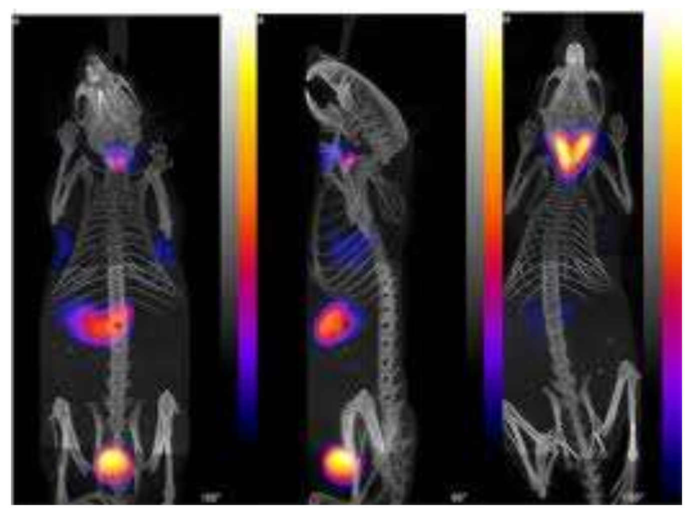
Christian Thibaudeau, *Sherbrooke Molecular Imaging*

HRRT High resolution brain scanner

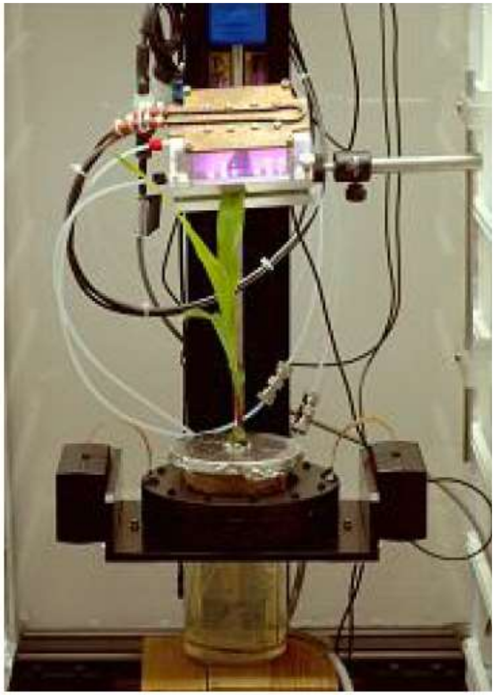




Small animal PET-CT



- plant imaging…



Budassi, MIC 2012

And long history of many other application-specific prototypes

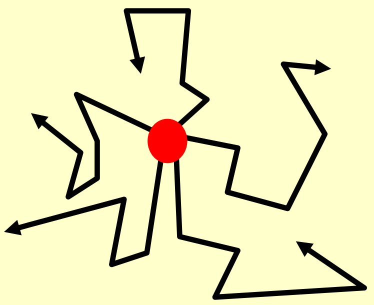
- Breast
- Prostate
- Brain

.. *but all commercial development aimed at whole body PET-CT systems*

Scanner spatial resolution

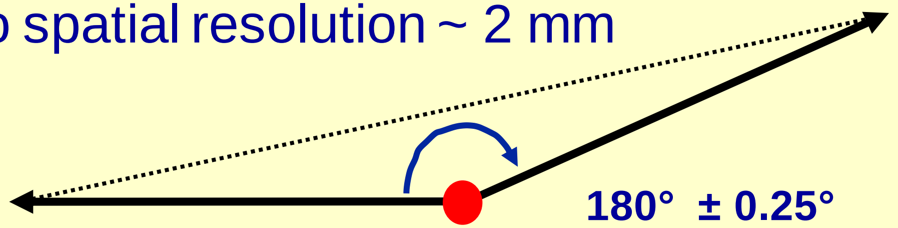
Positron range

- For ^{18}F contribution of positron range to spatial resolution is ~ 0.15mm



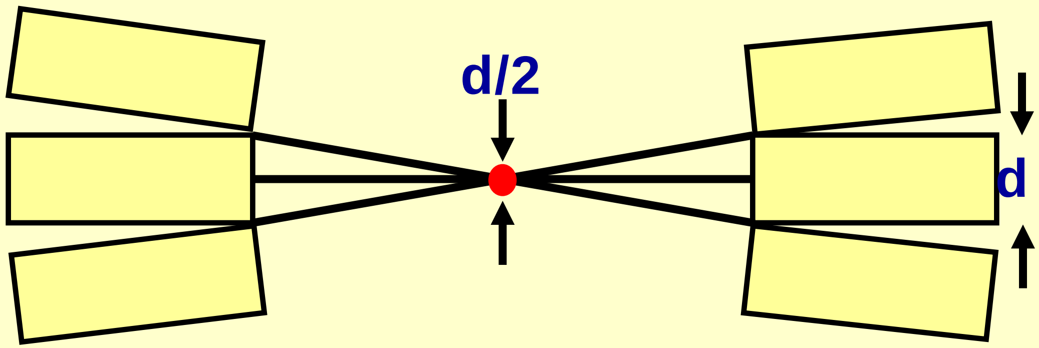
Acollinearity of annihilation gammas

- Magnitude of error increases linearly with diameter of scanner
- For 1m diameter contribution to spatial resolution ~ 2 mm



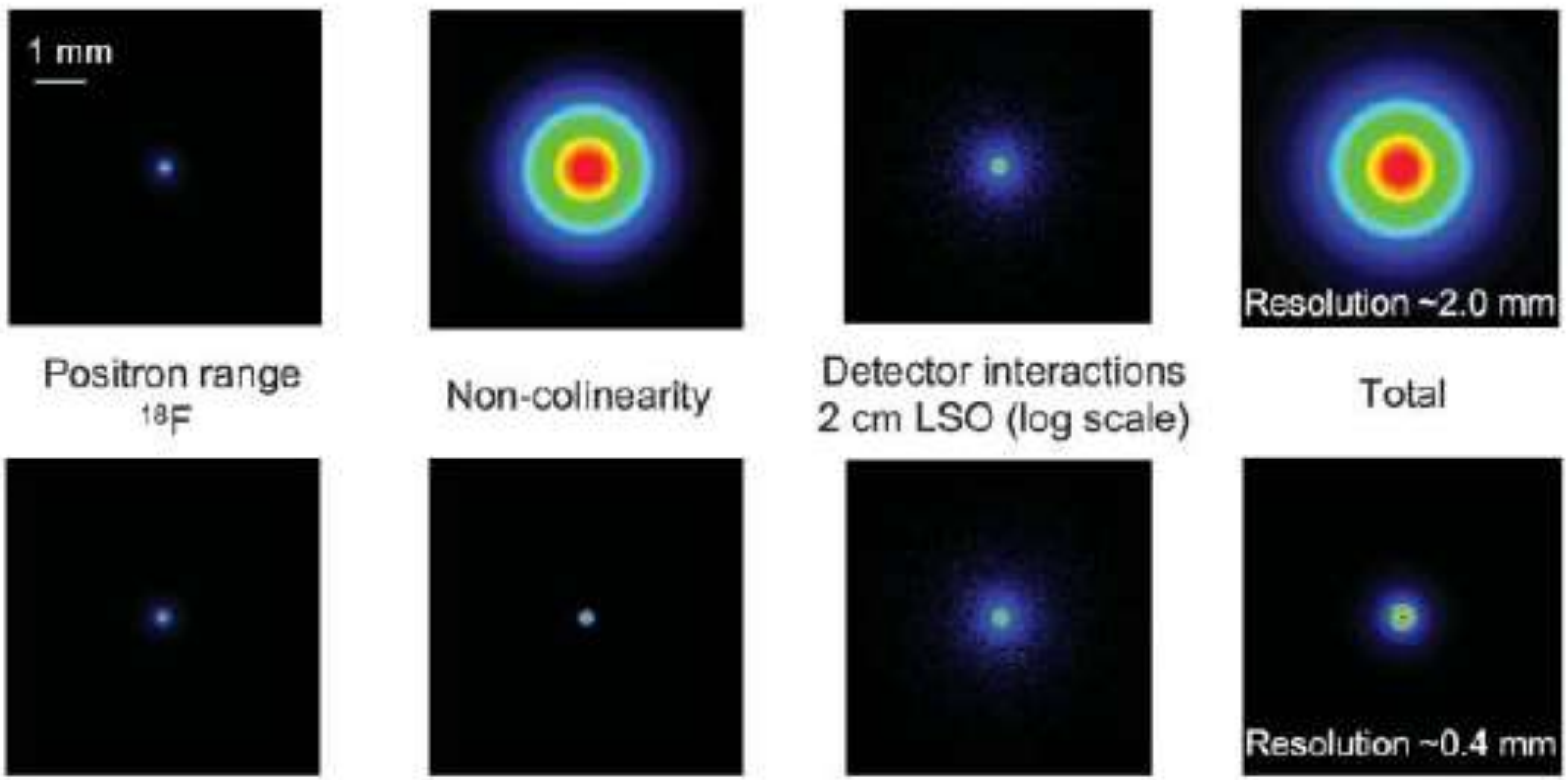
Detector element dimensions

- Contribution ~ d/2
- So typically 2-3 mm



Limits to resolution: contribution of physical factors

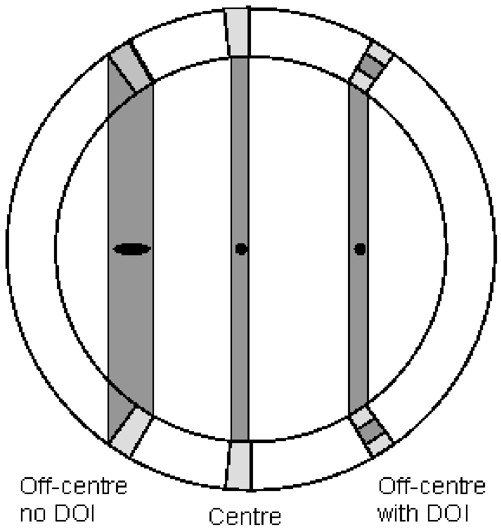
Clinical PET (80cm diameter) / ^{18}F

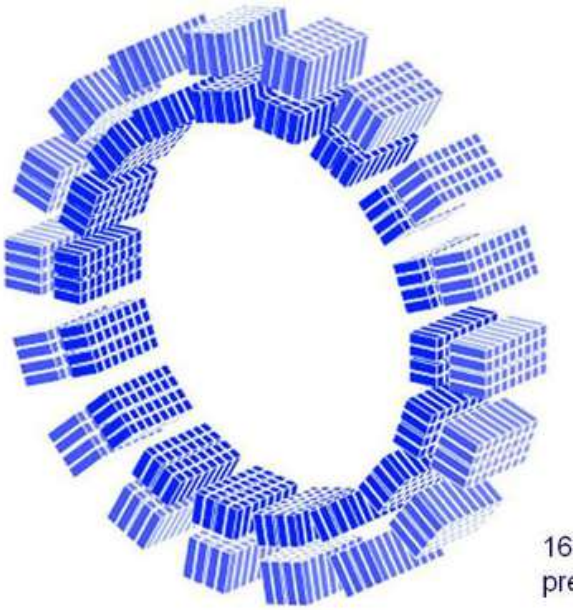


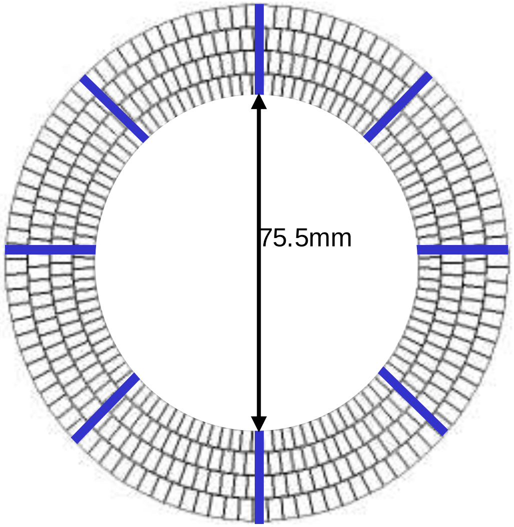
Small animal PET (8cm diameter) / ^{18}F

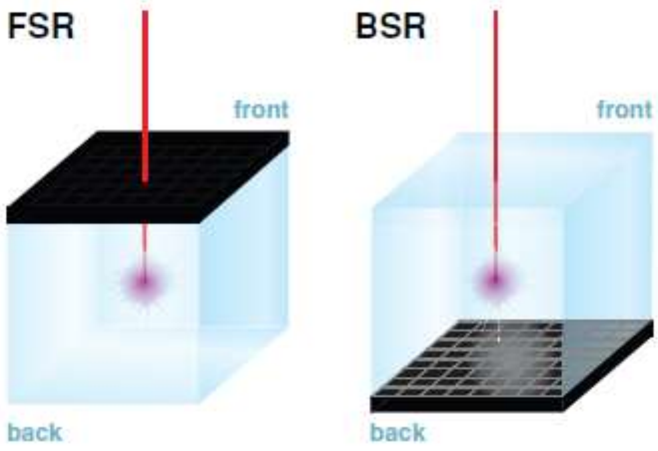
J R Stickel and S R Cherry, High resolution PET detector design: Modeling components of intrinsic spatial resolution, Phys Med Biol 50 (2), pp. 179-195. (2005).

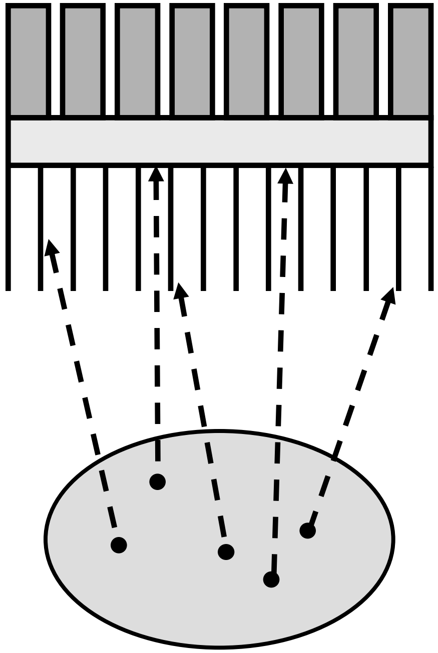
Depth of interaction effects

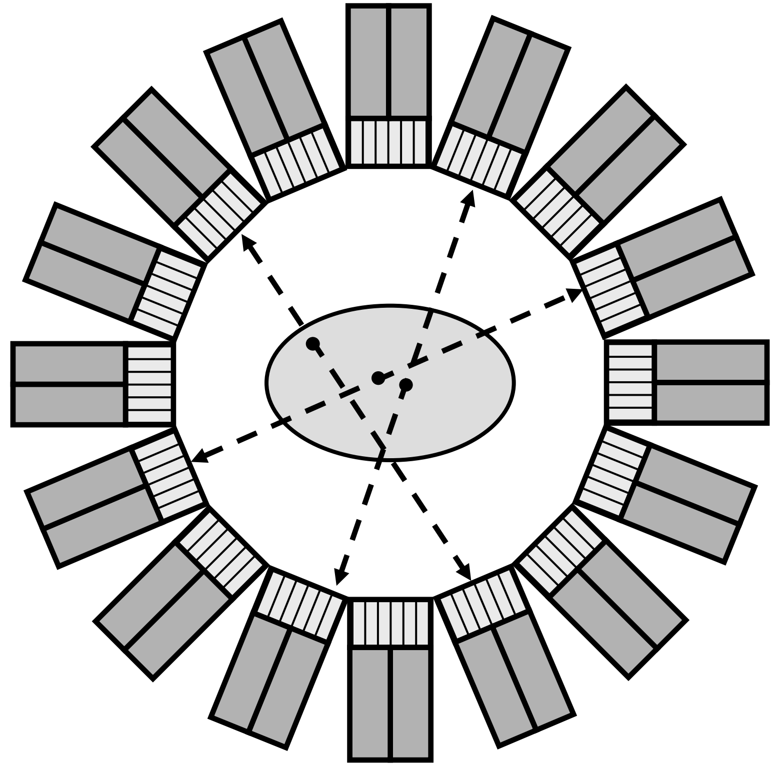












Collimated single photon system

Positron Emission Tomography

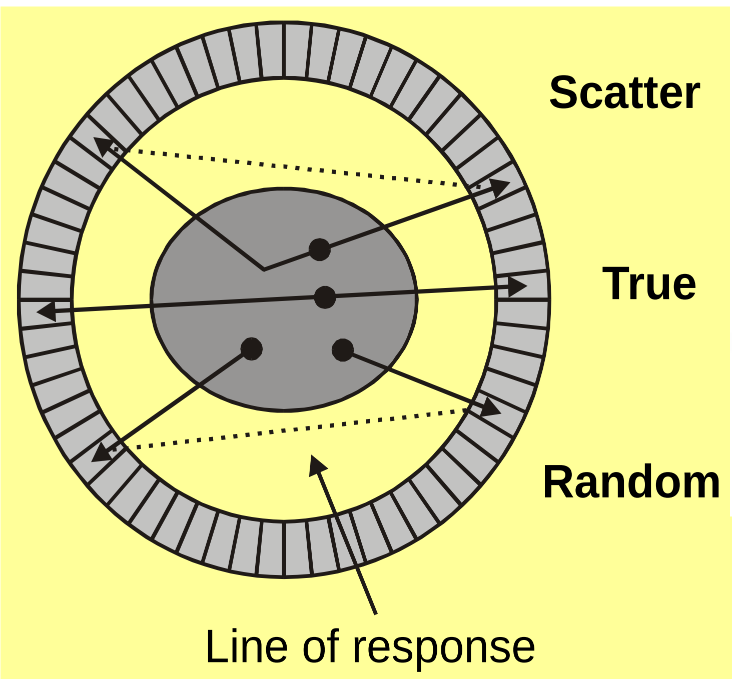
Absolute sensitivity ~ 0.05%

Absolute sensitivity ~ 0.5 – 5%

$\sim \Omega\varepsilon^2/4\pi$

Randoms and scatter

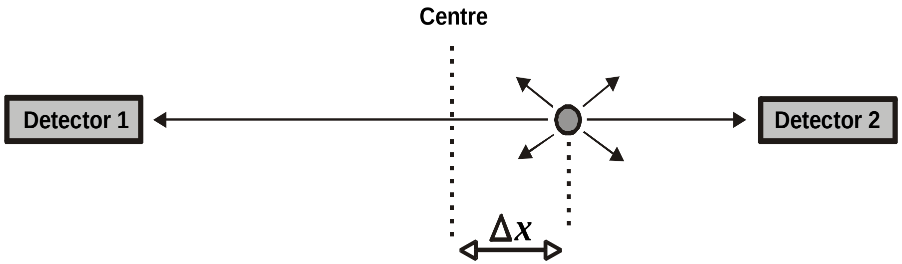
- Contribute background across image – easily (!) corrected
- Increased noise reduces image SNR
- Both randoms and scatter increase with patient size
- Randoms also increase with activity
- Energy and temporal resolution > improved SNR
- Many prototypes fail to consider these issues…



Standard
EU phantom

Same true counts but
additional 'fat' layer

Time of flight



$$\Delta t = 2\Delta x / c$$

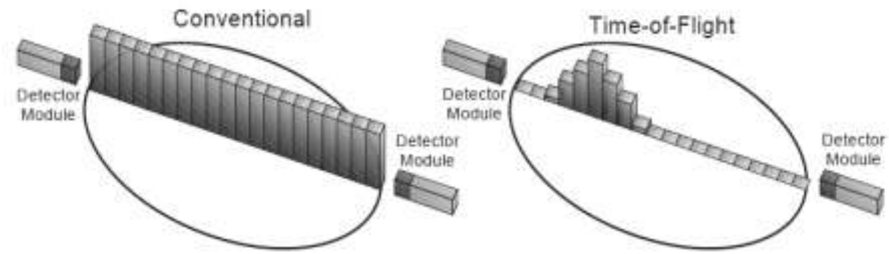
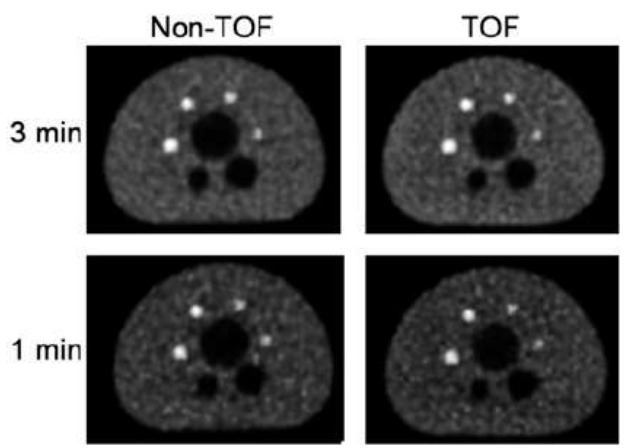


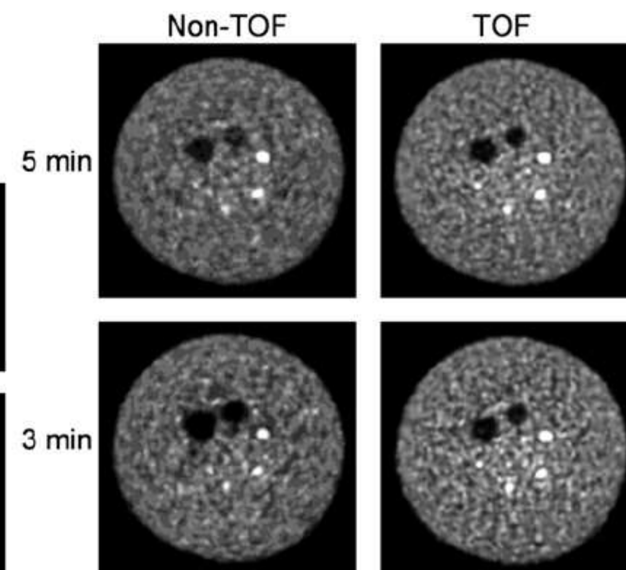
Figure 2: Time-of-Flight Reconstruction. With conventional reconstruction (shown on the left), all pixels along the chord are incremented by the same amount. With time-of-flight reconstruction (shown on the right), each pixel on the chord is incremented by the probability (as determined by the time-of-flight measurement) that the source is located at that pixel.

Bill Moses, LBLN - 51788

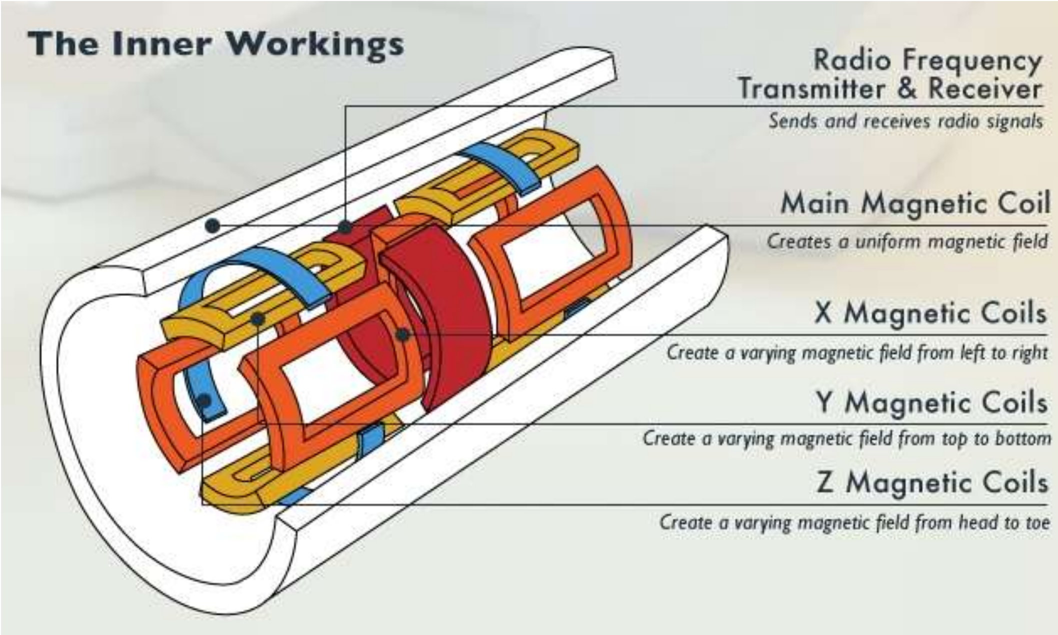
- 100ps >> 1.5 cm
- First tried in 1980s using BaF_2
- Now being revisited with LSO/SiPM ~ 350 ps
- Promises significant SNR improvements

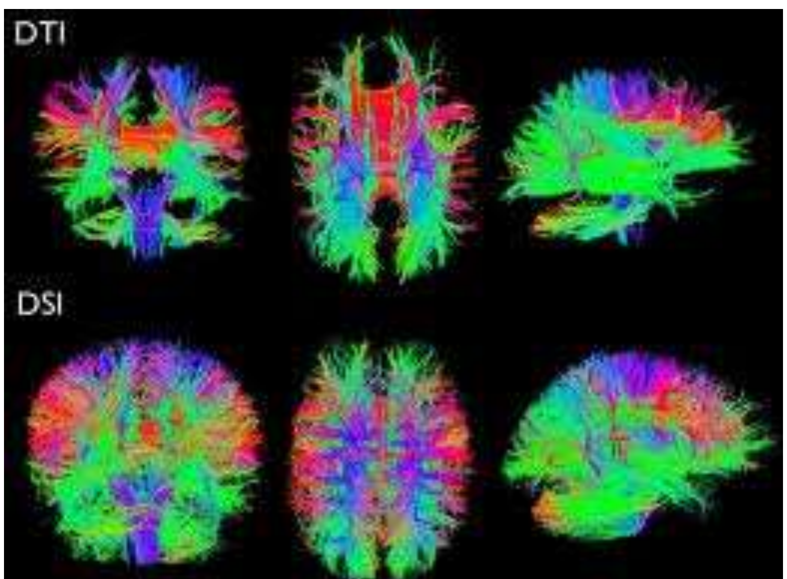
Philips Gemini ToF scanner





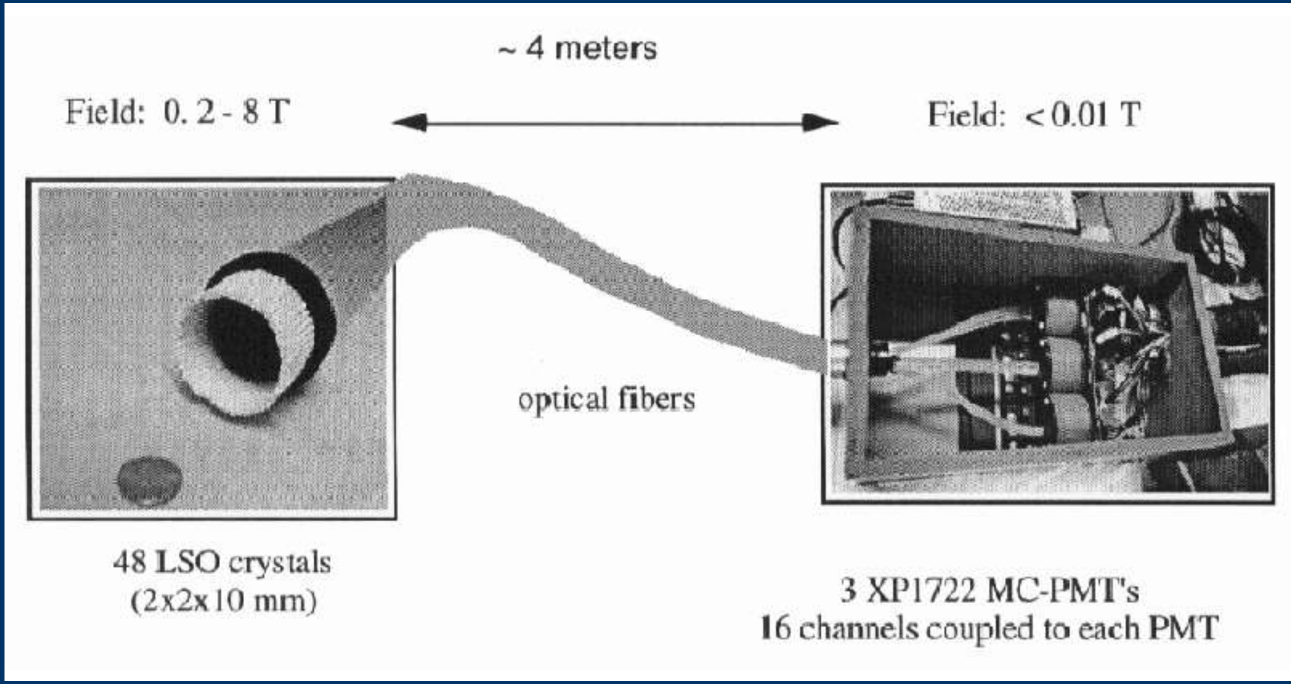
Surti et al, JNM 2007

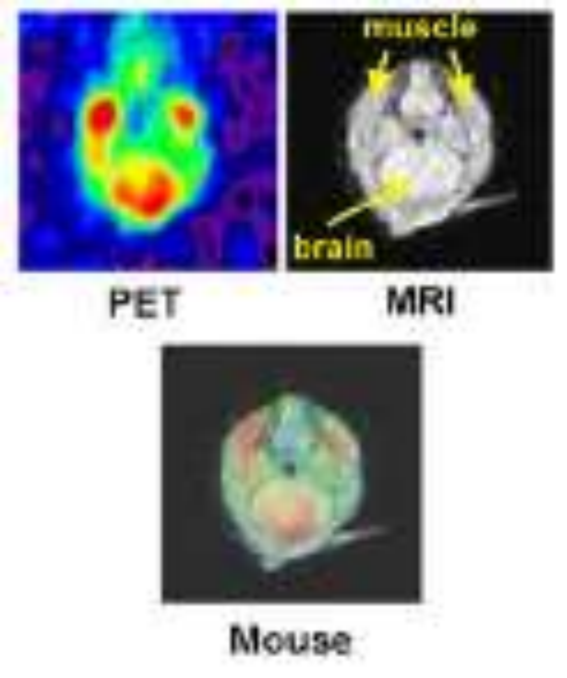

The Inner Workings
Radio Frequency Transmitter & Receiver
Sends and receives radio signals
Main Magnetic Coil
Creates a uniform magnetic field
X Magnetic Coils
Create a varying magnetic field from left to right
Y Magnetic Coils
Create a varying magnetic field from top to bottom
Z Magnetic Coils
Create a varying magnetic field from head to toe


DTI
DSI

First PET-MR images – 1997 !

Yiping Shao, Simon R Cherry, Keyvan Farahani, Ken Meadors, Stefan Siegel, Robert W Silverman and Paul K Marsden, *"Simultaneous PET and MR imaging",* Phys. Med. Biol. **42** (1997) 1965–1970.



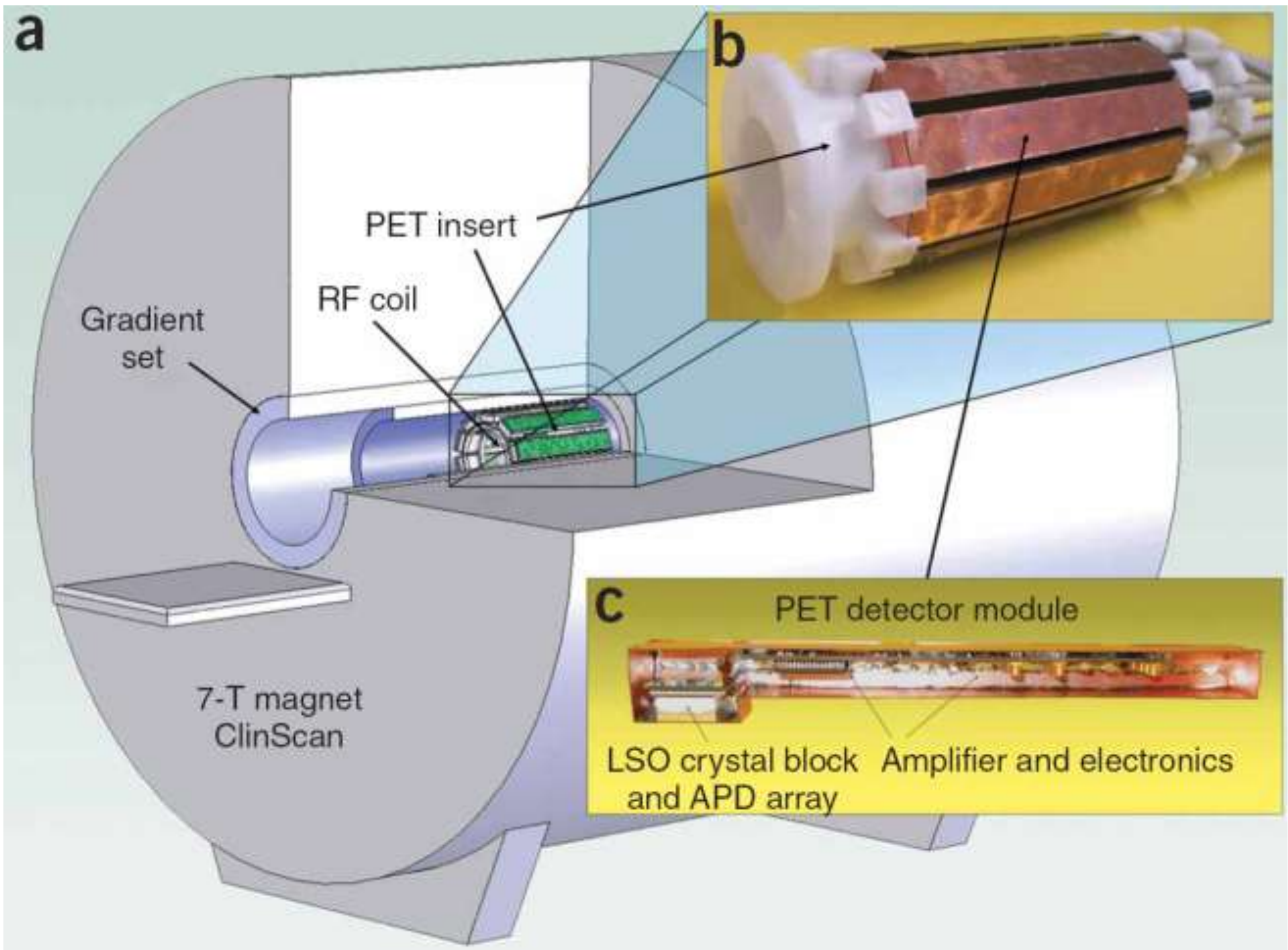


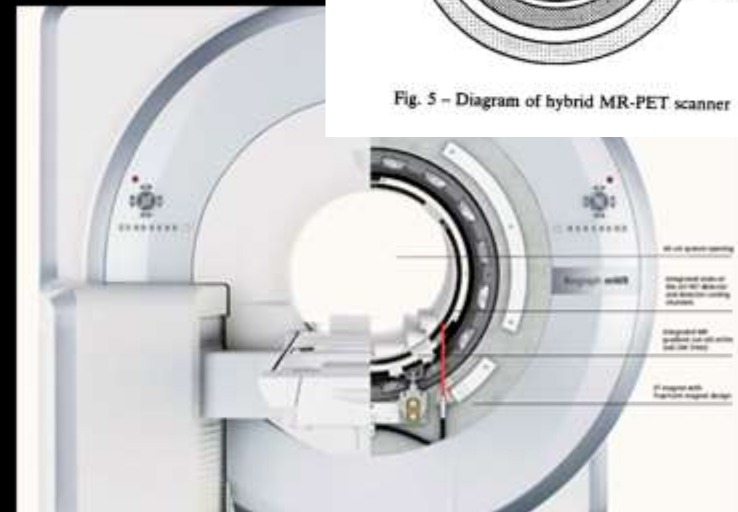
nature medicine

Simultaneous PET-MRI: a new approach for functional and morphological imaging

Martin S Judenhofer[1], Hans F Wehrl[1], Danny F Newport[2], Ciprian Catana[3], Stefan B Siegel[2], Markus Becker[4], Axel Thielscher[5], Manfred Kneilling[6], Matthias P Lichy[1], Martin Eichner[7], Karin Klingel[8], Gerald Reischl[9], Stefan Widmaier[4], Martin Röcken[6], Robert E Nutt[2], Hans-Jürgen Machulla[9], Kamil Uludag[5], Simon R Cherry[3], Claus D Claussen[1] & Bernd J Pichler[1]

NATURE MEDICINE VOLUME 14 | NUMBER 4 | APRIL 2008 459





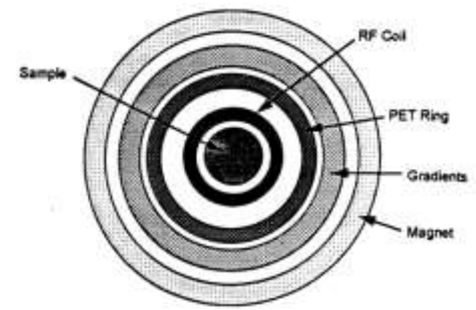
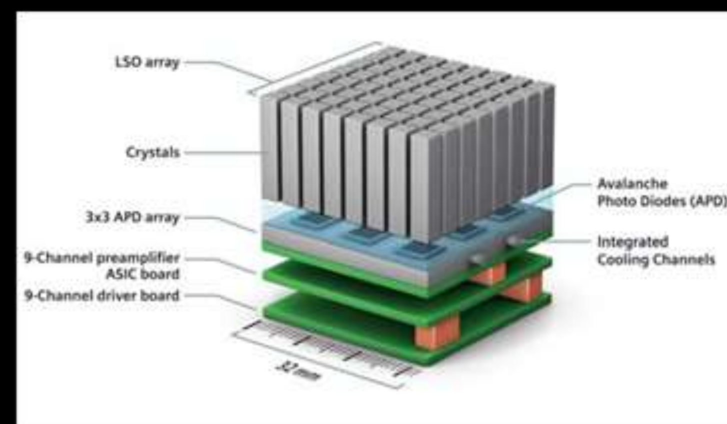
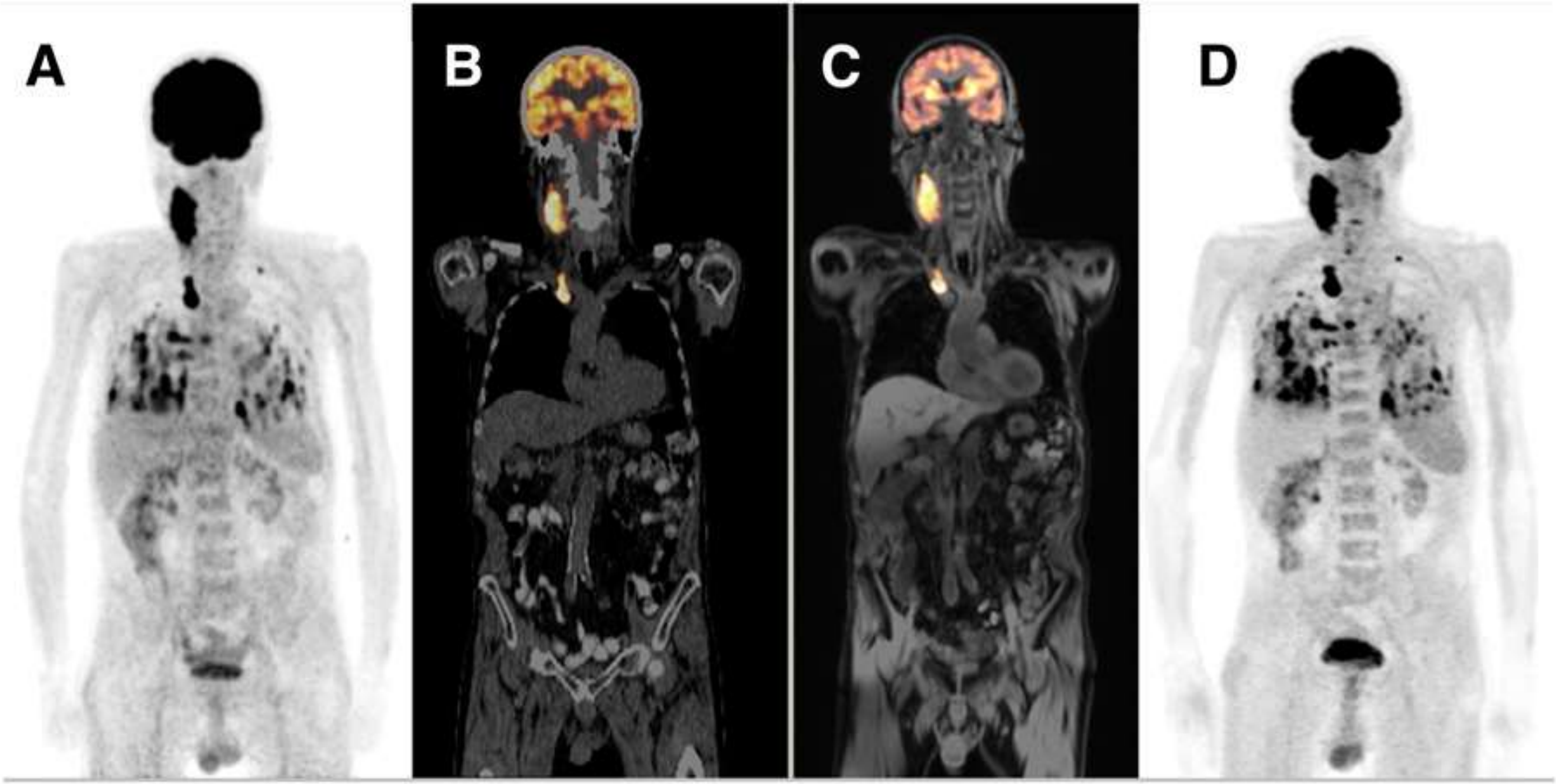


Fig. 5 – Diagram of hybrid MR-PET scanner



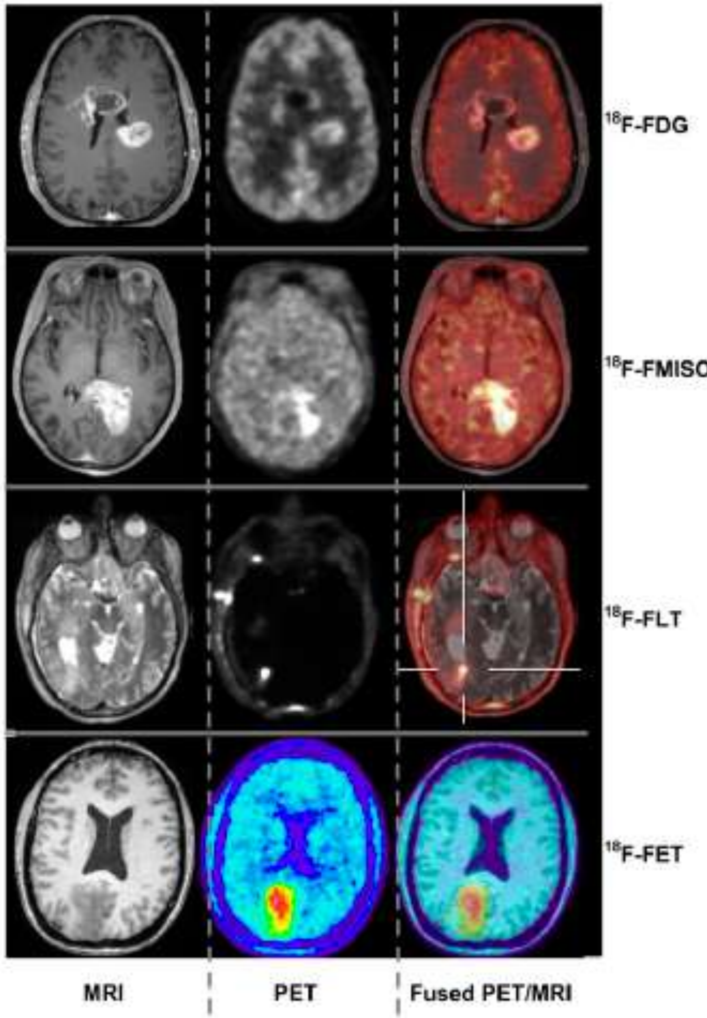
Applications – clinical imaging

PET-CT PET-MR

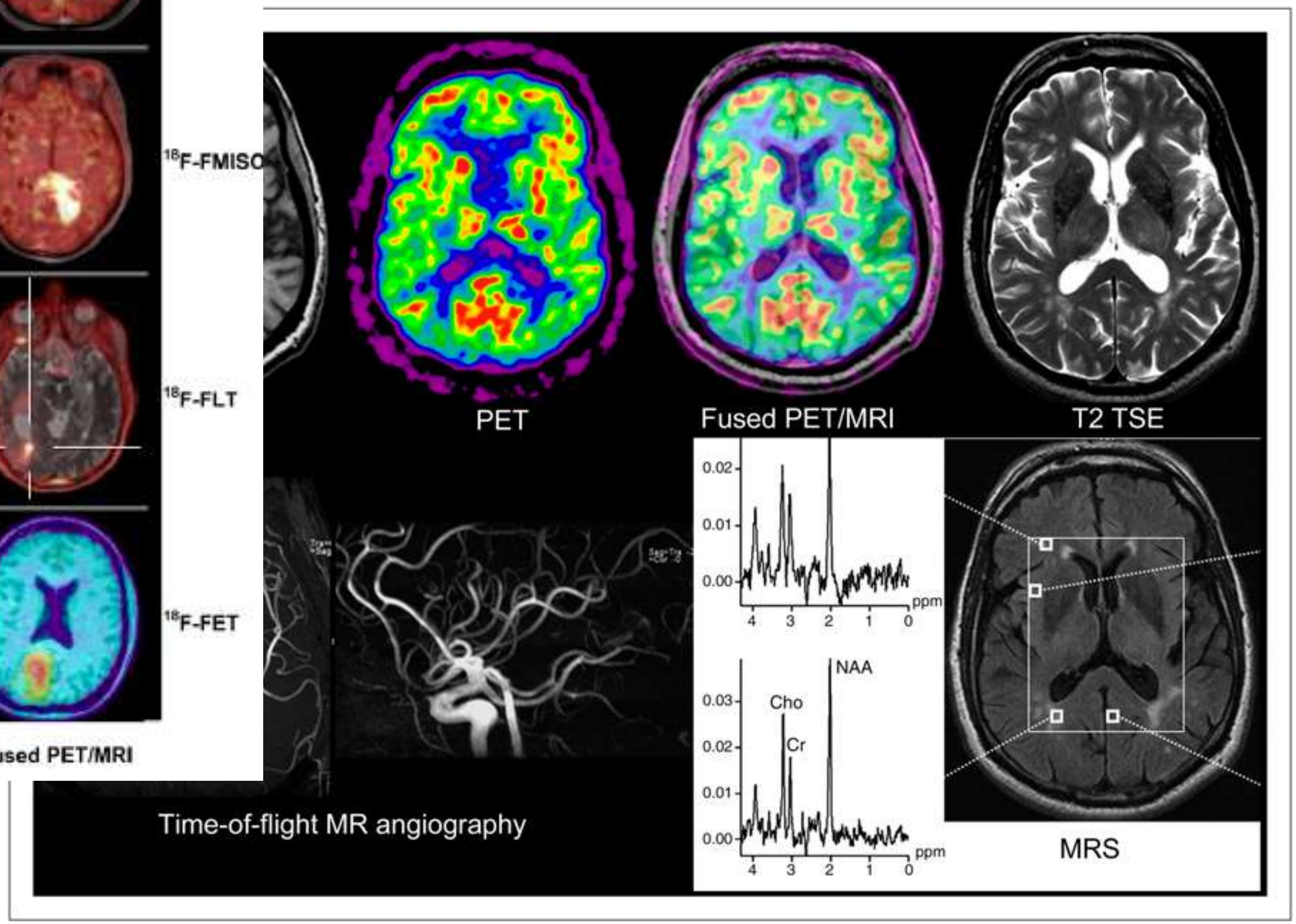


Drzezga et al, 2013

Applications - brain



Hans Herzog, Julich

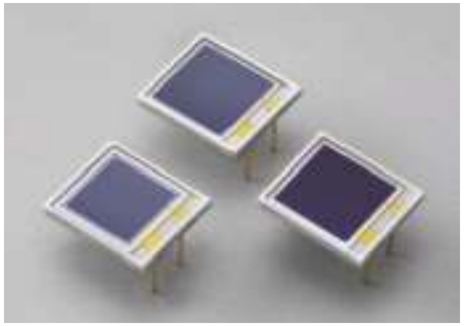


Schlemmer et al, Tuebingen

New photodetectors

Avalanche photodiodes (APD)

- Immune to large magnetic fields
- PET-MR
- Very low gain cf PMTs
- Too slow for ToF
- Poor temp stability

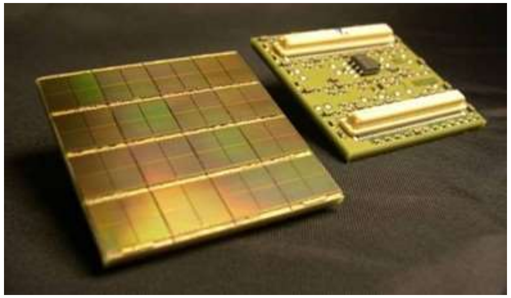


Silicon photomultipliers (SiPM)

- High gain
- Very fast – ToF PET > 100ps ?
- Better temp stability
- Potential successor to PMT

Digital silicon photomultipliers (dSiPM)

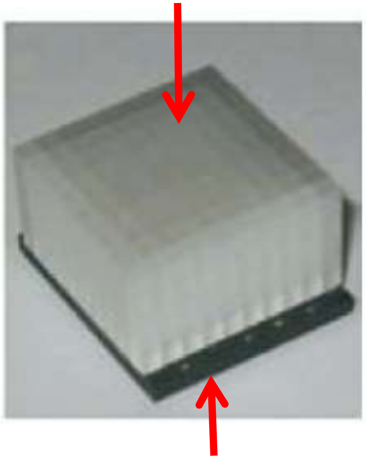
- Electronics/detector on same chip
- Completely digital design
- Digital PET scanner



PMT

SSPD

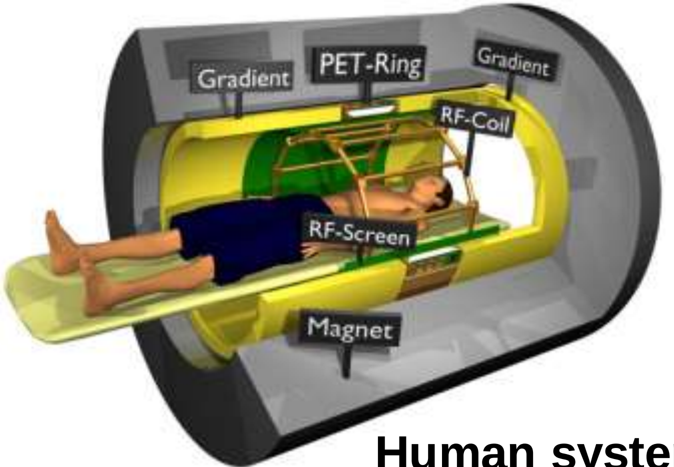
Crystal array



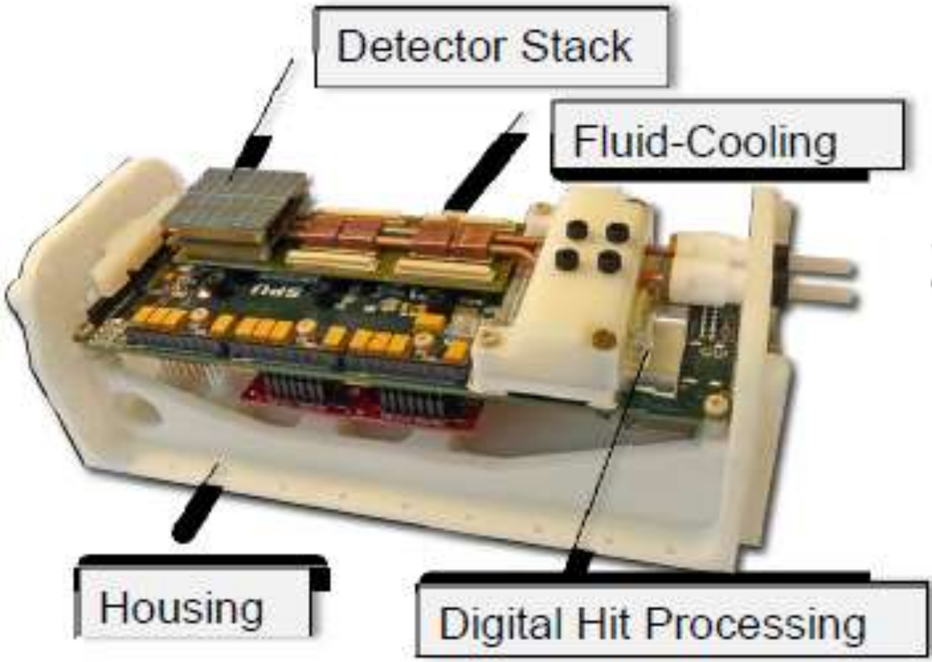
Photodetector

EU Framework 7 *'Hyperimage'* project

- New MR-compatible SiPM detector technology
- MR-compatible time-of-flight PET
- MR-based attenuation correction
- Motion compensation
- Example applications in cancer and the heart
- 8 European partners 2008-2011



Human system



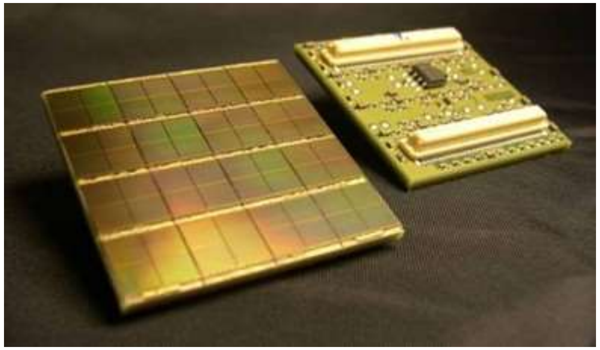
SiPM–based detector module

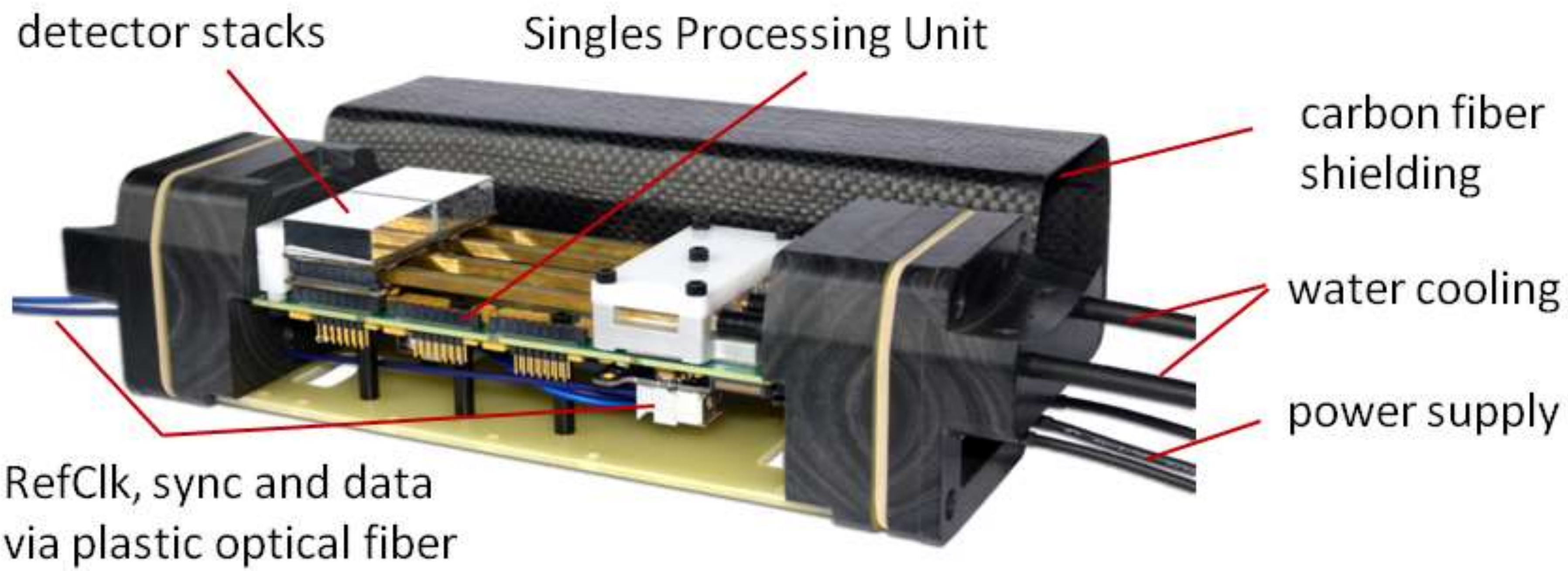
Preclinical system

MkII system with digital SiPM detectors

Digital silicon photomultiplier (dSiPM)

- Binary cell outputs summed digitally
- Electronics/detector on same chip
- Completely digital design
- Excellent performance
- Easy to use



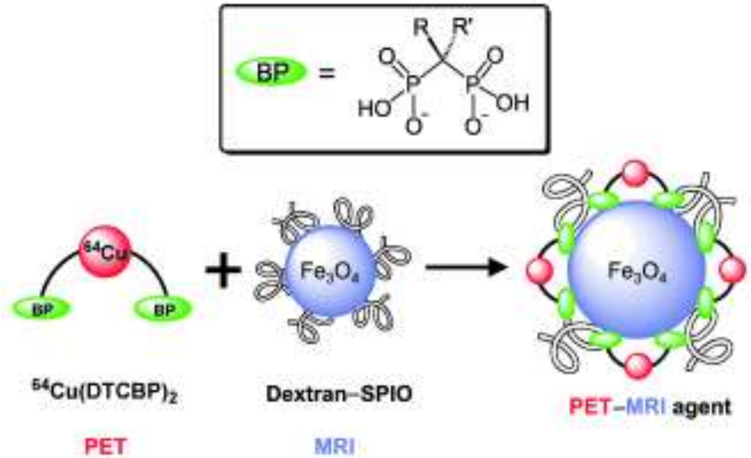


(Unfortunately carbon fibre RF shielding not suitable for human systems..)

KCL Medical Engineering Centre/Sublima F7 projects

Dynamic Study of Dual labelled PET/MR Probe

^{64}Cu(DTCBP)2-Endorem



(R. T. M de Rosales et al. Angew. Chem. Int. Ed. 2011, 50, 5509–5513)

Simultaneous dynamic study

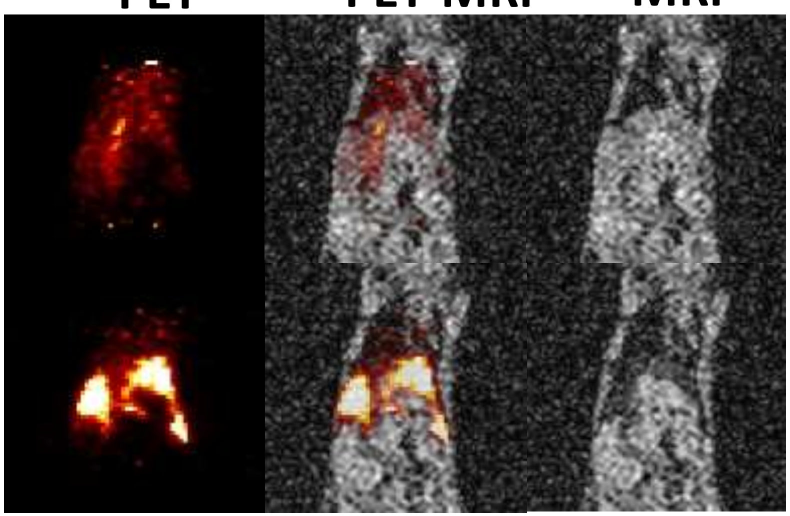
PET: 20 MBq ^{64}Cu frame time 10 – 60 s

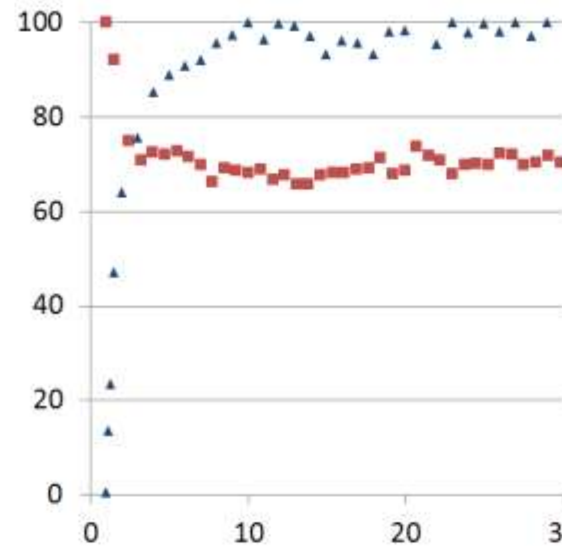
MR: Single slice gradient echo, iron oxide nanoparticle (negative contrast), ΔT ~ 45s

PET **PET-MRI** **MRI**

60–120 sec

360–420 sec





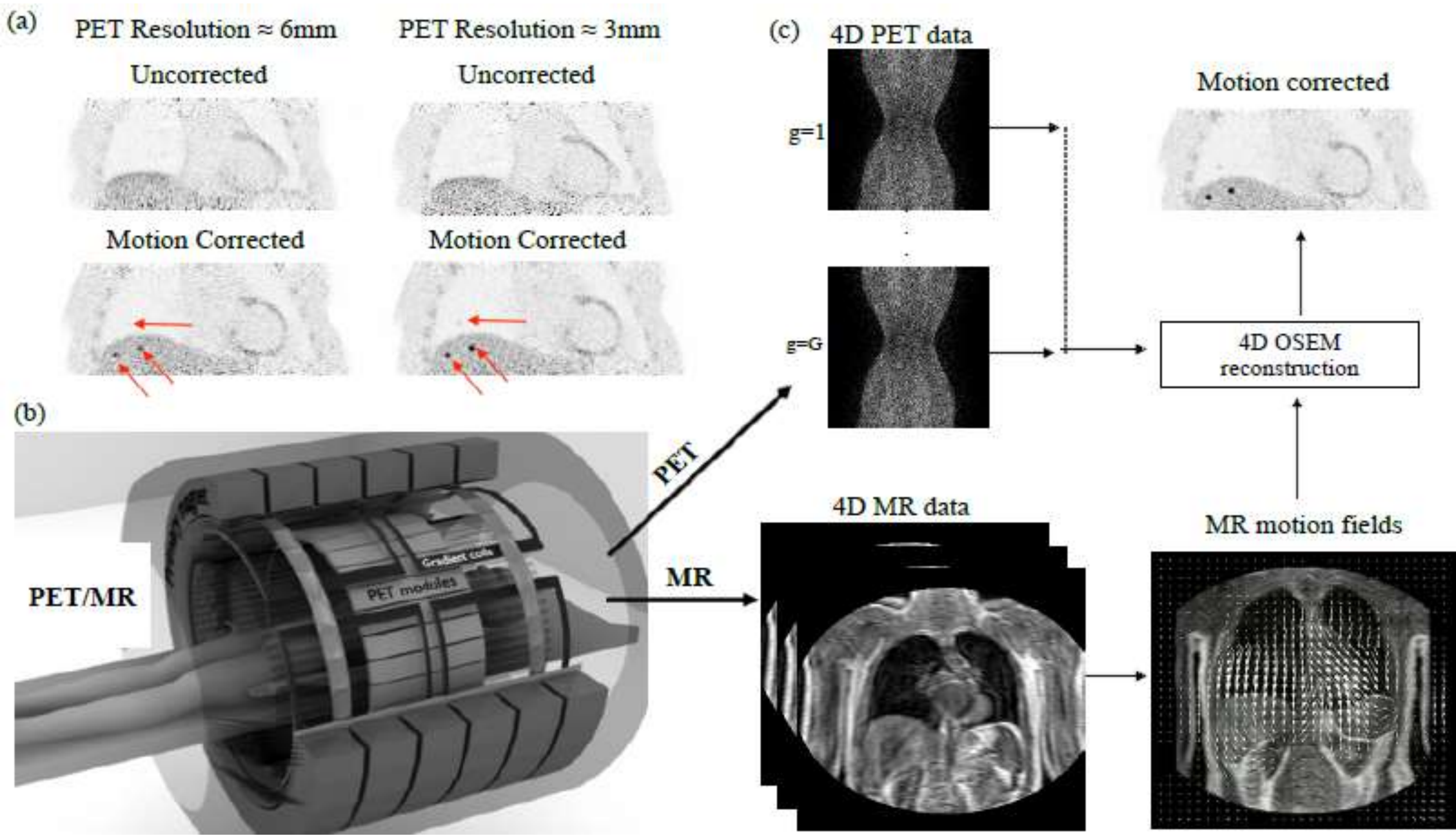
PET uptake

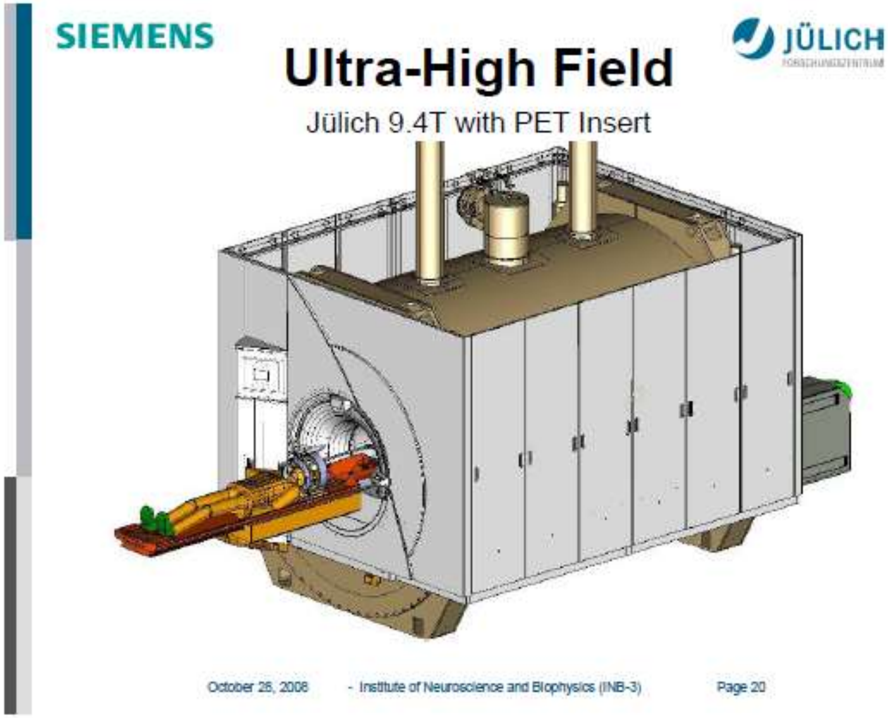
MR signal loss

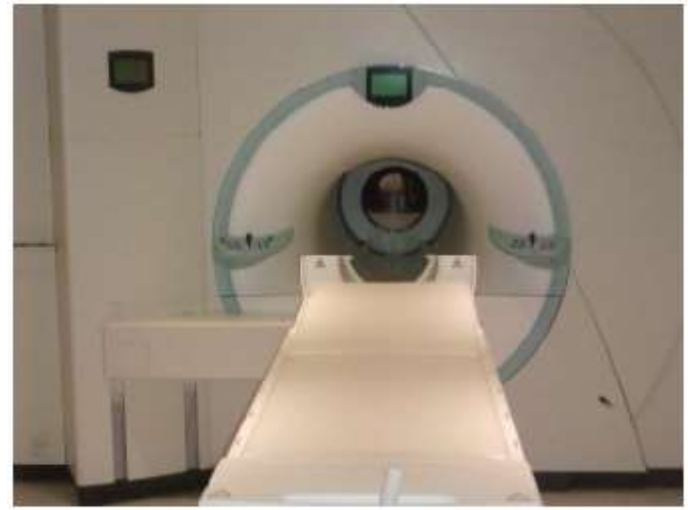
Minutes p. i.

KCL

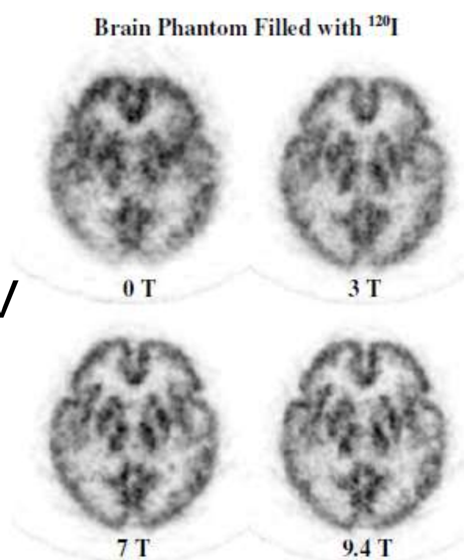
Dynamic MR correct PET for effects of patient motion

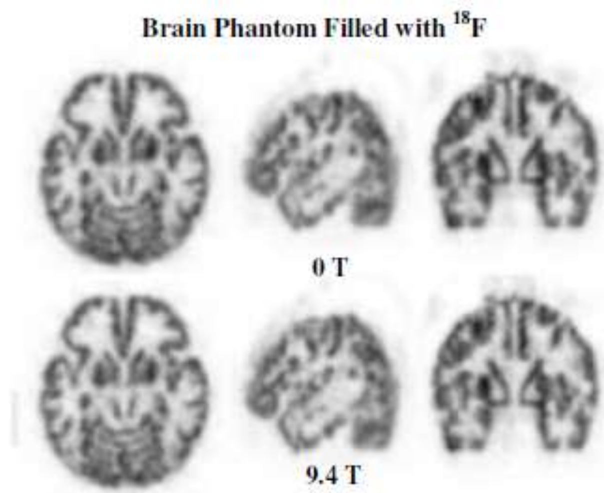






^{120}I – 4 MeV





^{18}F - 0.6 MeV

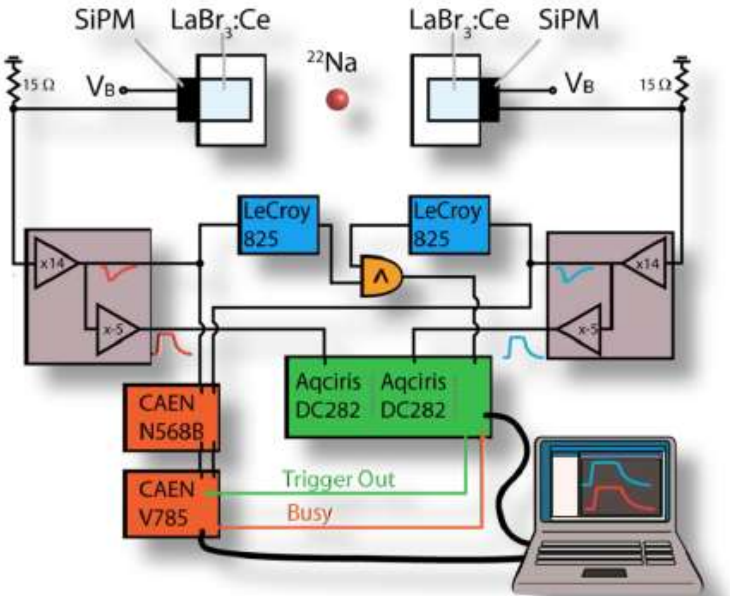
Jon Shah, Hans Herzog, Julich

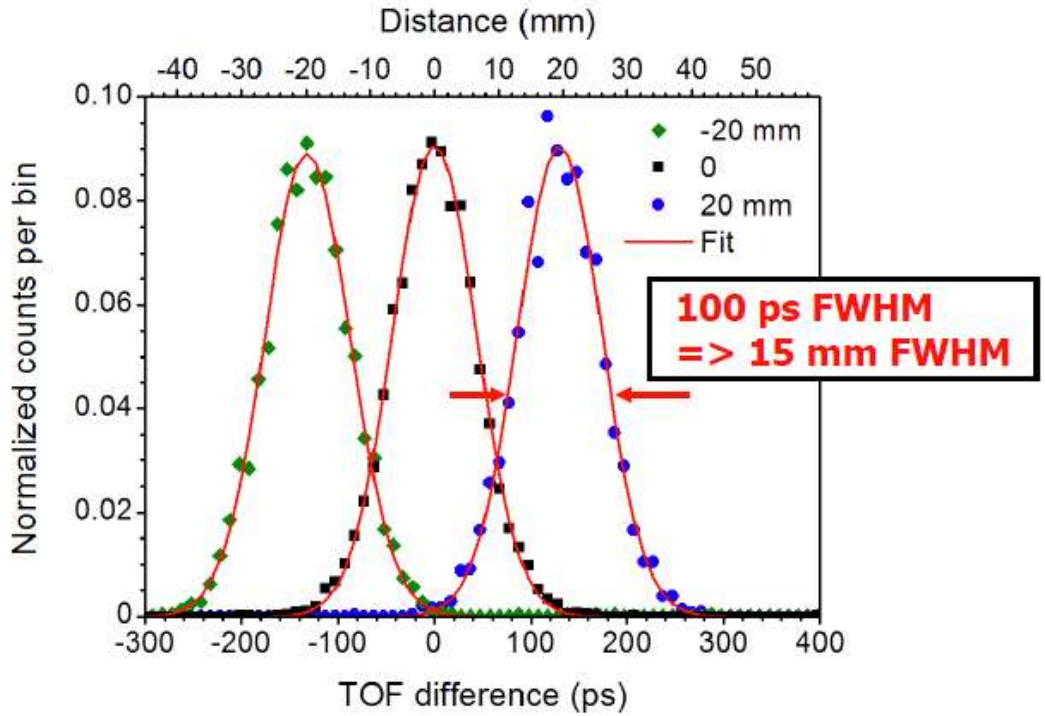
Philips digital SiPM PET-CT

In lab, 100 ps barrier has been broken

Made possible by the combination of:

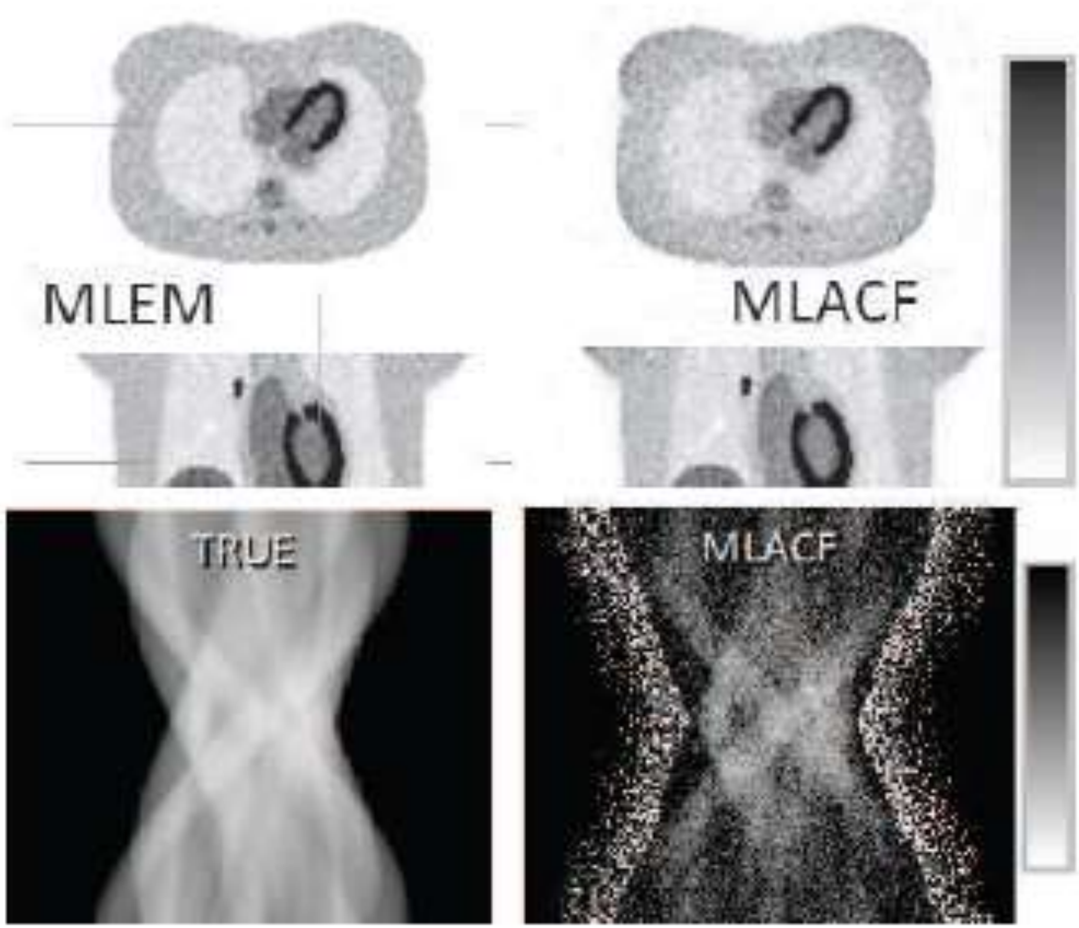
- Small $LaBr_3$:Ce(5%) crystals (3 mm x 3 mm x 5 mm)
- Silicon Photomultipliers (Hamamatsu MPPC-S10362-33-050C)
- Digital Signal Processing (DSP)



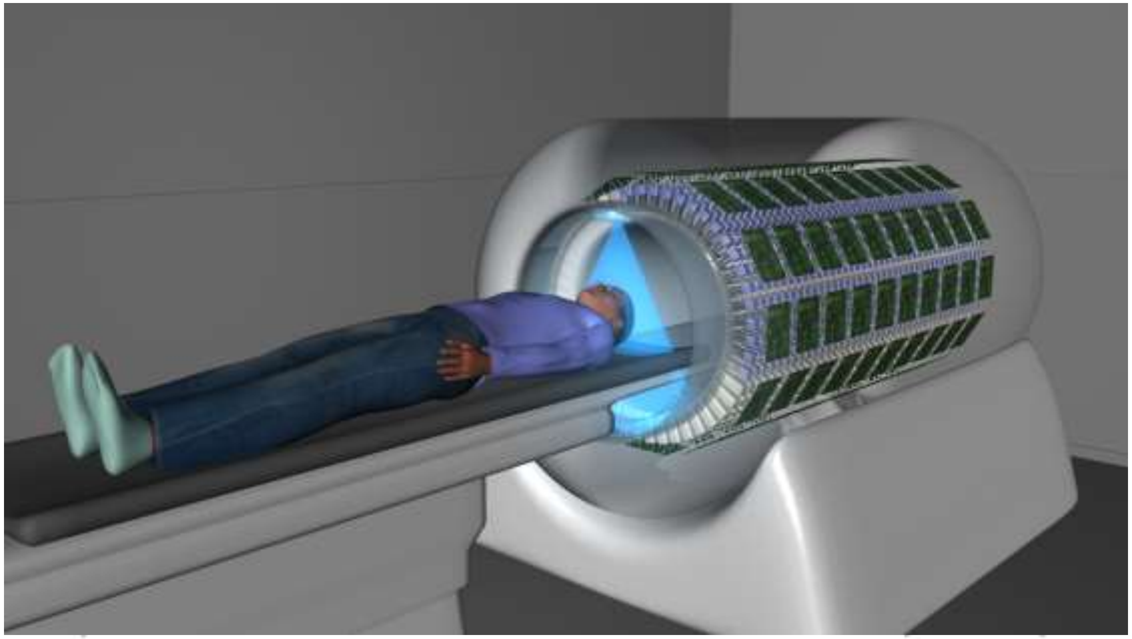


ML-reconstruction for TOF-PET with simultaneous estimation of the attenuation factors

Johan Nuyts [1], Ahmadreza Rezaei[1], Michel Defrise[2]

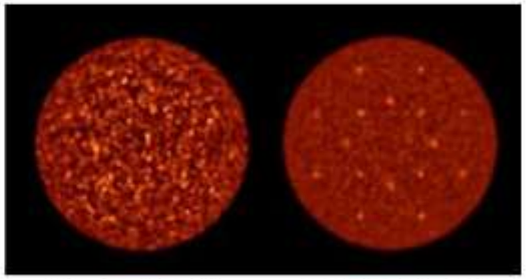


EXPLORER Consortium

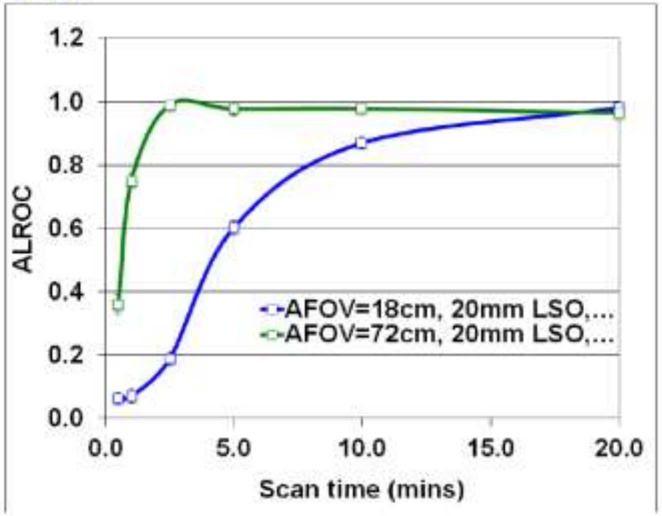


RESULTS

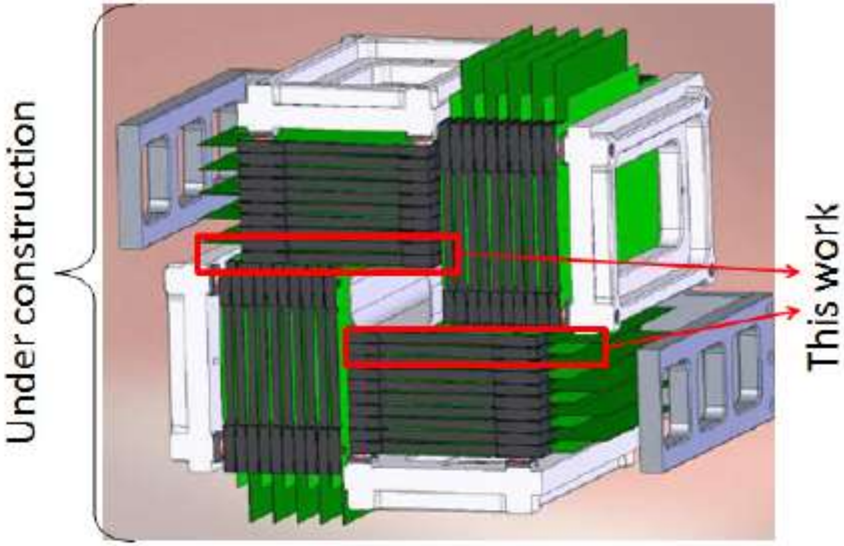
Images for the 2.5 min scans are shown to the left. ALROC curves are shown on right. The long AFOV scanner achieves the same ALROC value at 2.5 mins that the conventional scanner achieves at 20 mins.

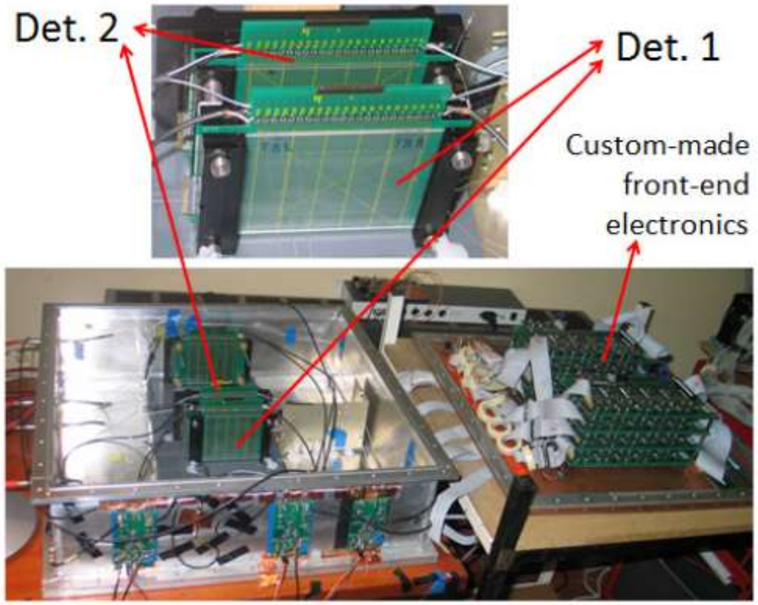


18 cm AFOV 72 cm AFOV



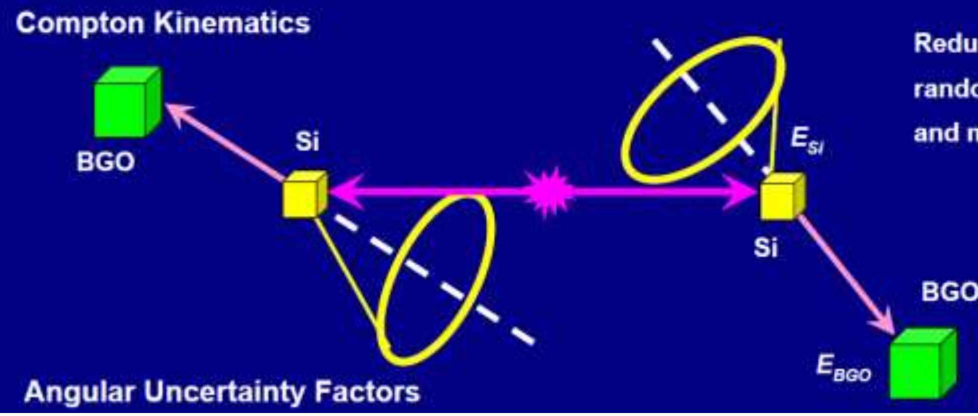
RPC-based small animal PET prototype





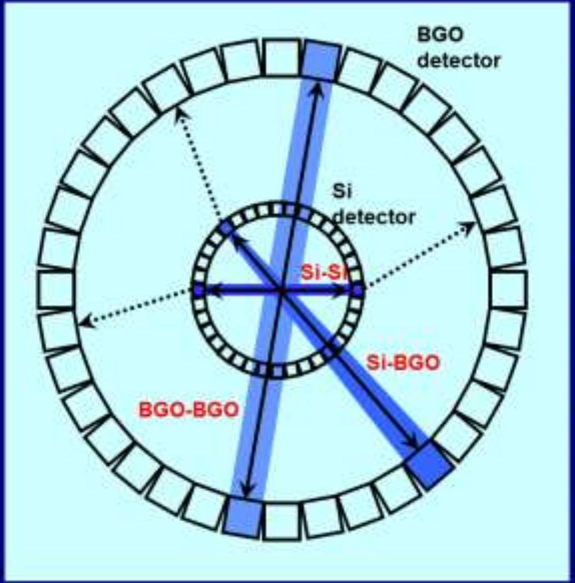
Paulo Martins

Compton Kinematics



Reduction of scatter,
random,
and misclassified events

Compton PET Concept



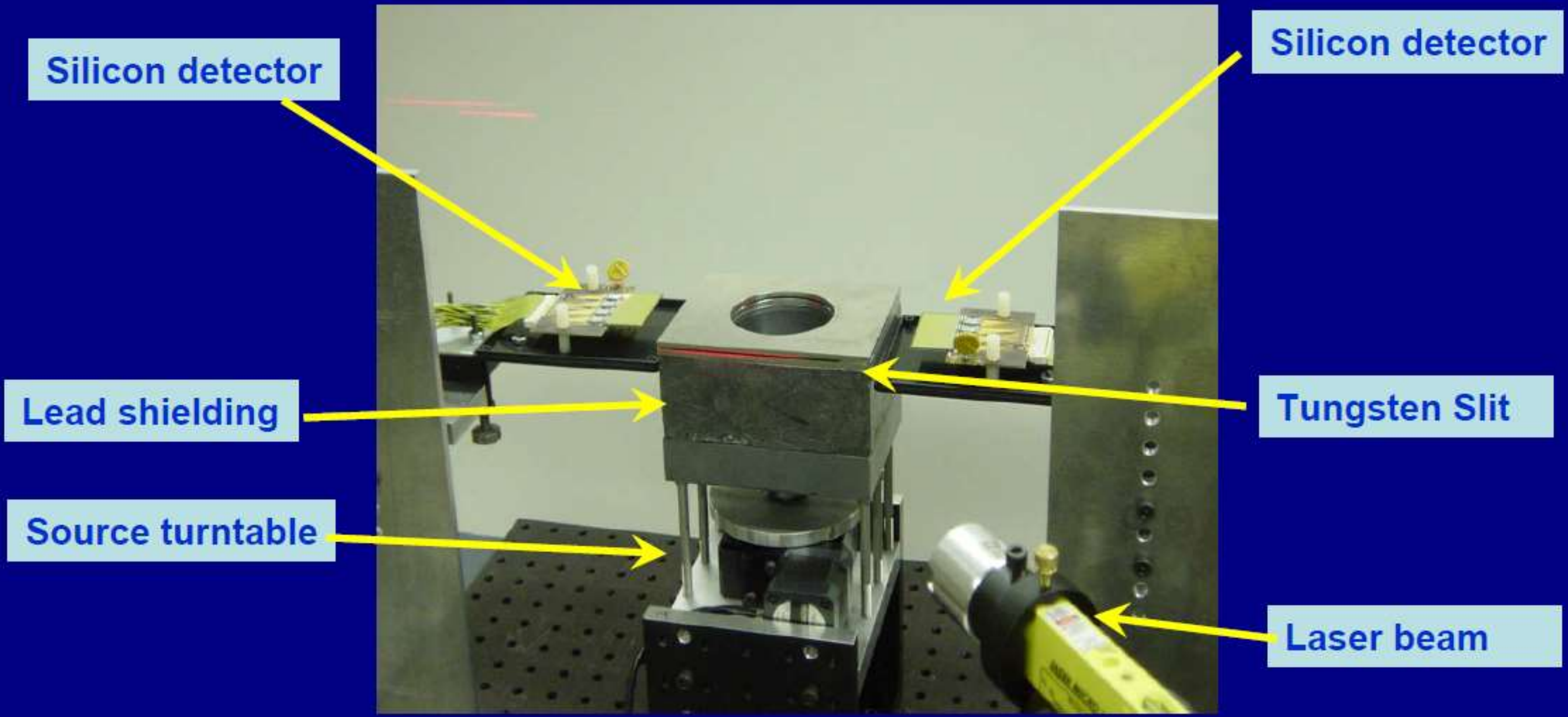
Uses two sets of detectors: low resolution and high

Low resolution detectors can be conventional PET or small animal PET scanner

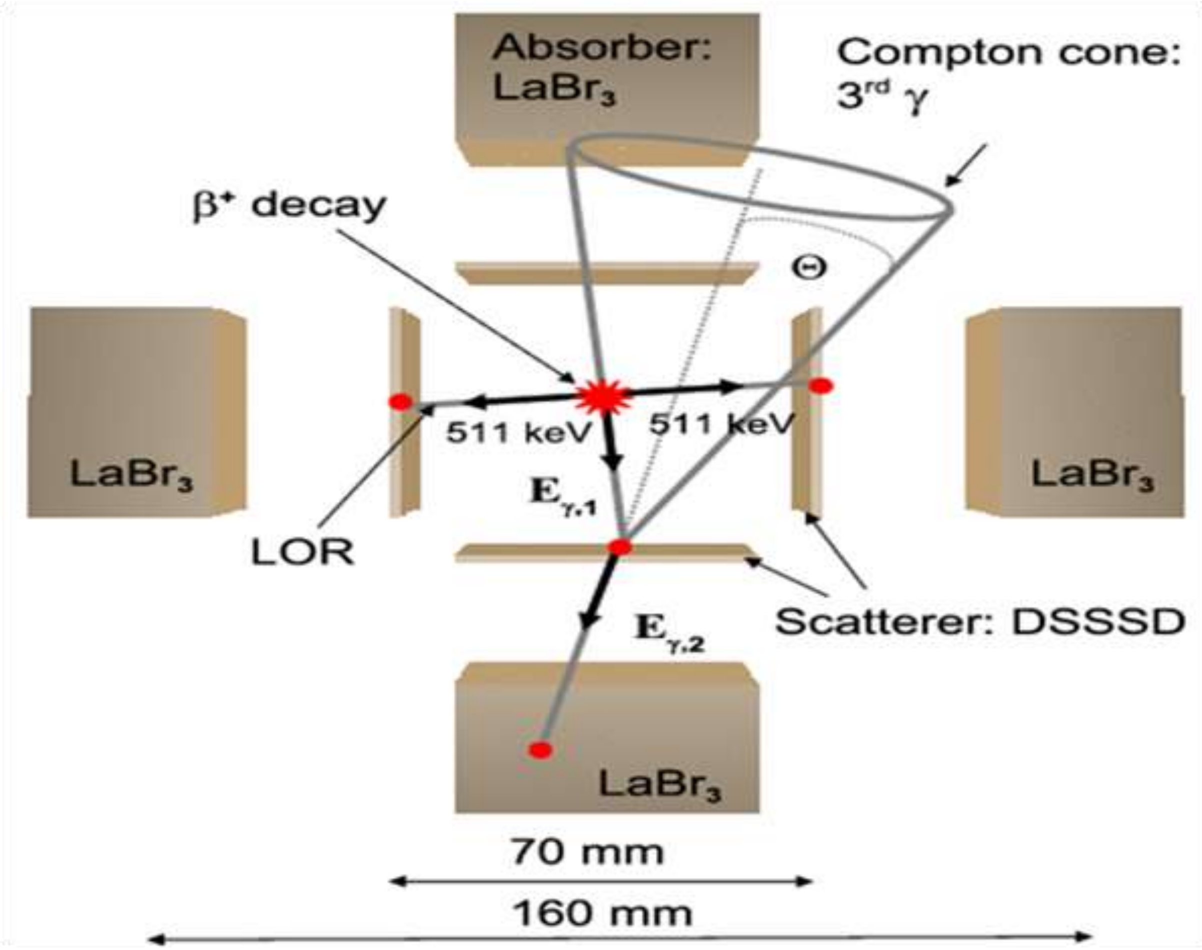
High resolution detectors 3D stack of position-sensitive solid-state detectors

Resolution to challenge positron range

Setup and Alignment



BGO detectors, electronics not shown



Peter Thirolf, Munich

Challenges/Opportunities

- *New technologies, notably SiPM/ToF, are now finding their way into clinical systems*
- *ToF promises significant performance improvements (but its not there yet..)*
- *Applications still based around whole body PET-CT*
- *Potential of PET-MR still to be demonstrated/exploited*
- *Possible re-emergence of dedicated hi-res brain systems*
- *No role currently for solid state detectors…*
- *Future possibilities from exploiting Compton kinematics..*

Thankyou...!

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Hyperimage

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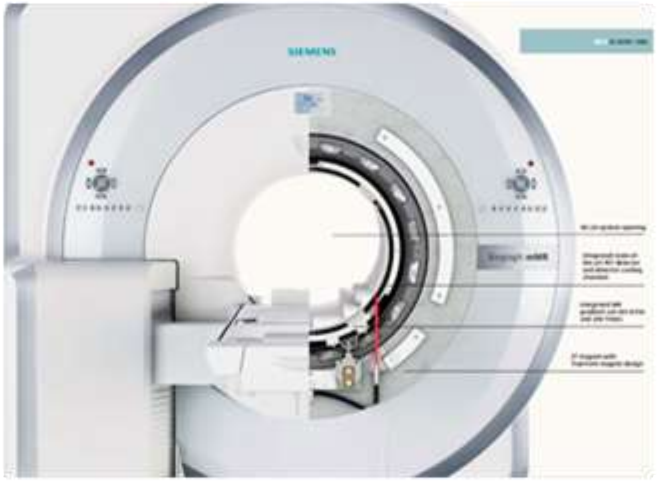

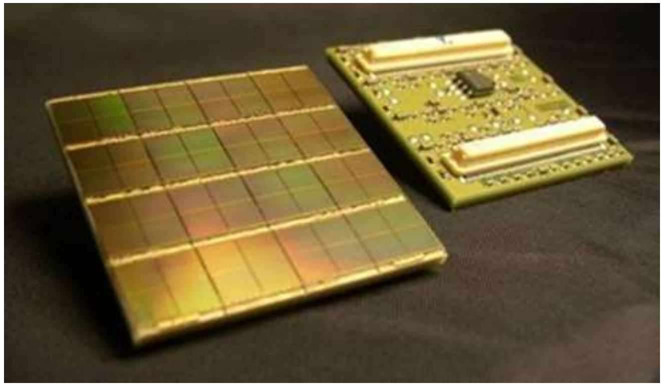

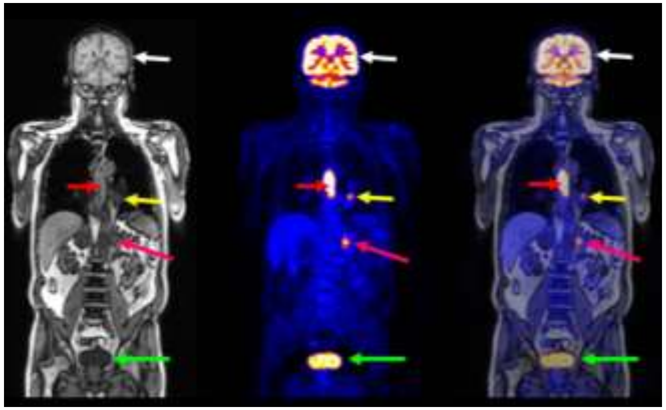

STFC Particle Physics Department
Rutherford Appleton Laboratory - 3 Sept 2014