FP 7 Collaborative Project

Novel MR-compatible PET detectors for simultaneous PET/MRI imaging

FP7-HEALTH-2009-single-stage

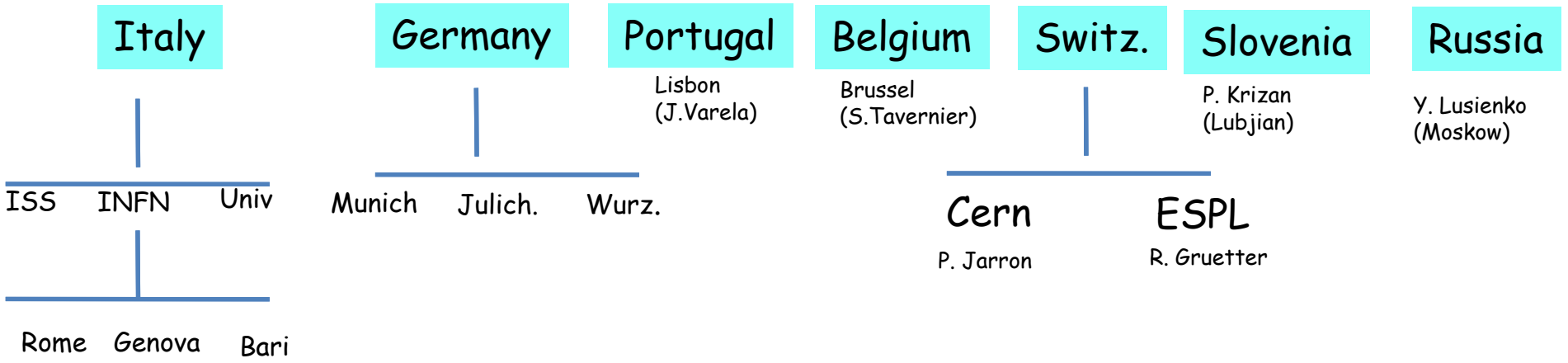
-Scope

-Issues

-Actions

-Deadline(s)

FP7 PET-MRI



Industries

Siemens ST MRI

France? (ST)

Spain ?

The Istituto Superiore di Sanità (ISS) is the leading technical and scientific public body of the Italian National Health Service. Its activities include research, control, training and consultation in the interest of public health protection.

Department of Cell Biology and Neurosciences

Department of Environment and Primary Prevention

Department of Food Safety and Veterinary Public Health

Department of Haematology, Oncology and Molecular Biology

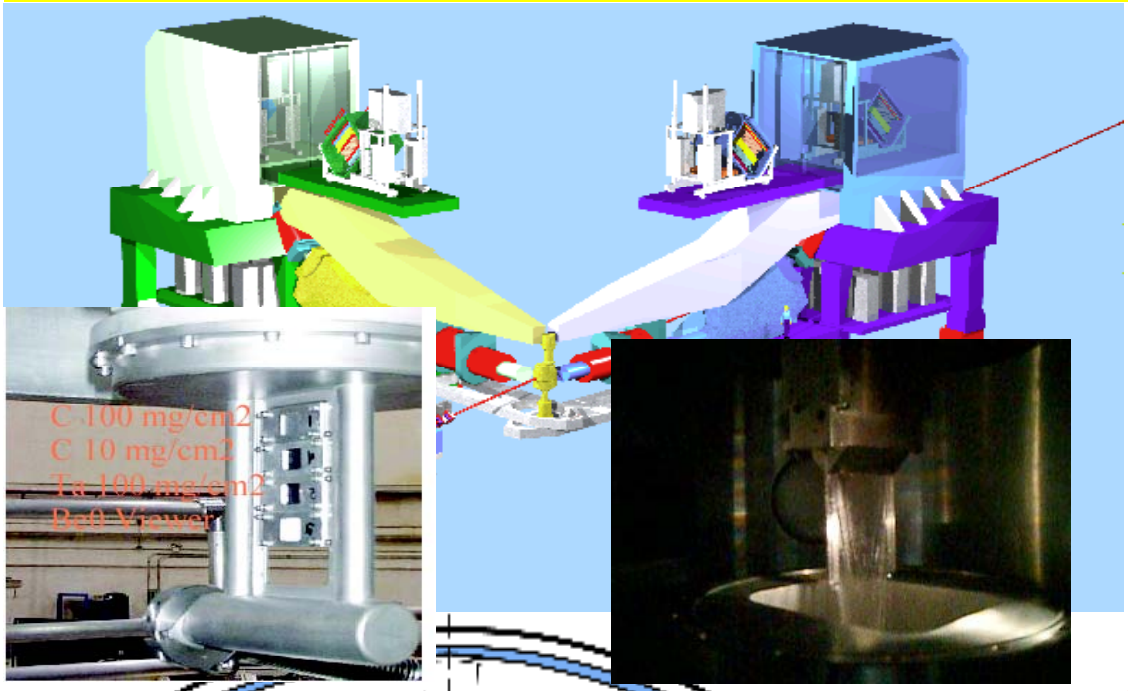
Department of Infectious, Parasitic and Immune-Mediated Diseases

Department of Technology and Health ←

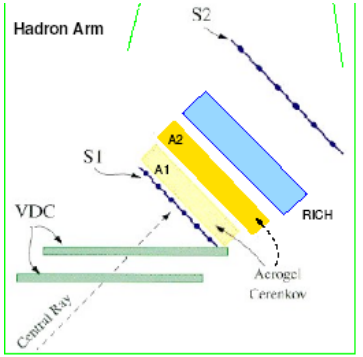
Department of Therapeutic Research and Medicines Evaluation

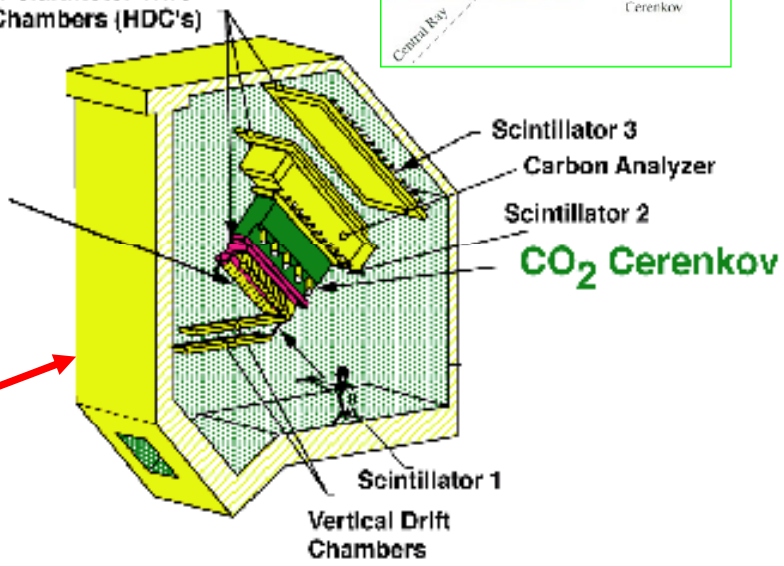
Hall A - Two High Resolution Spectrometers

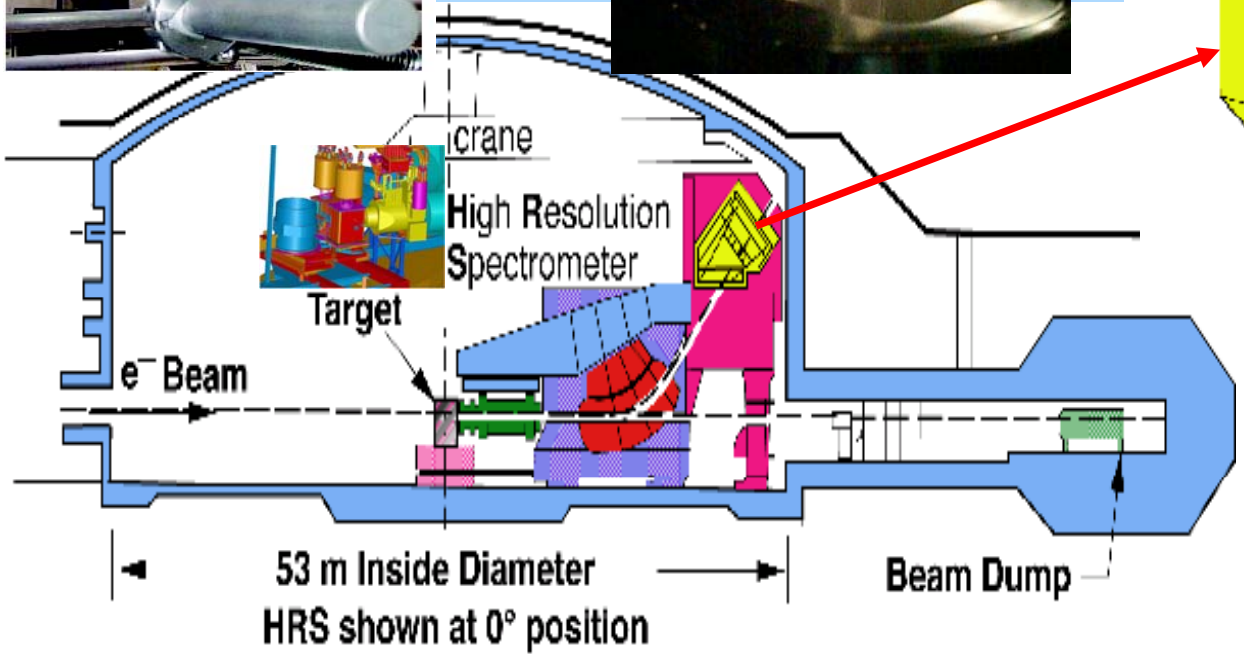
QDQ - Momentum Range: 0.3 -4 GeV/c $\Delta p/p$: 1 x 10-4 - Δp = =-5% - $\Delta\Omega = 5 - 6$ mr



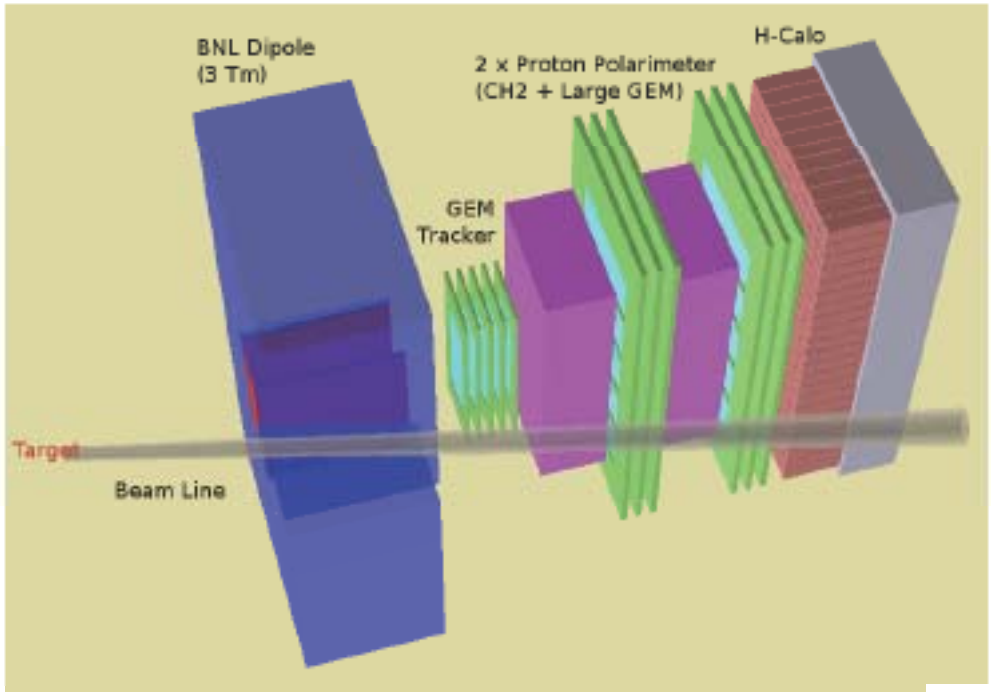
Polarimeter Wire Chambers (HDC's)

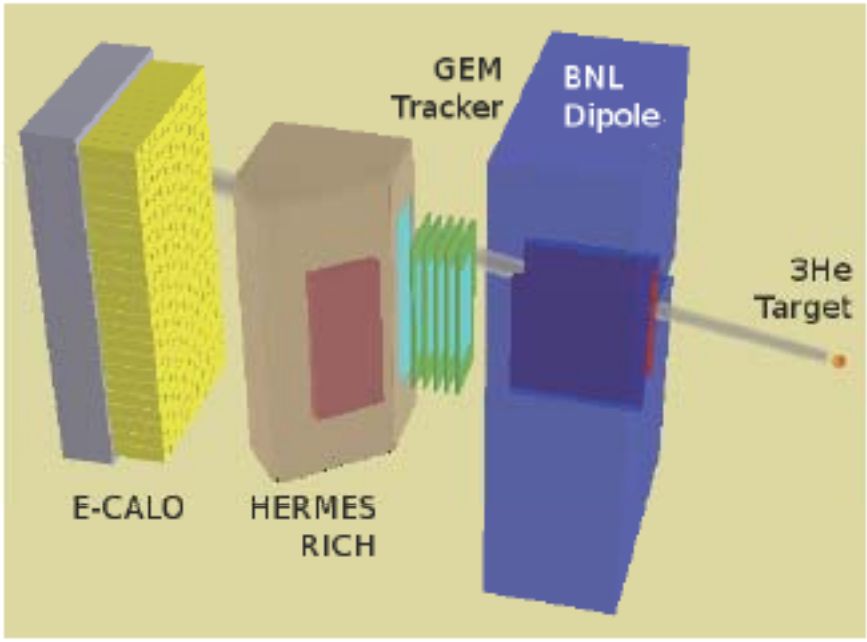






1 (+1) Cherenkov threshold aerogels + RICH in the hadron spectrometer + septum magnet


BNL Dipole
(3 Tm)
2 x Proton Polarimeter
(CH2 + Large GEM)
H-Calo
GEM
Tracker
Target
Beam Line


GEM
Tracker
BNL
Dipole
3He
Target
E-CALO
HERMES
RICH

High Resolution, High Sensitivity Detectors

key parameters

SNR (and contrast)

(spatial resolution)

they are correlated !

$$SNR = \frac{S - BKG}{\sqrt{S}}$$

S = counts in ROI,
BKG = background

$$IC = \frac{Max - BKG}{Max}$$

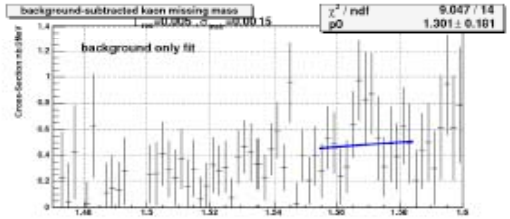
Max = max. counts in tumor ROI
BKG = average

$$DRF = n(r,z) = \int dxdyP(x,y)PSF\left\{\left[(x-r)^2 + y^2\right]^{1/2}, z\right\}$$

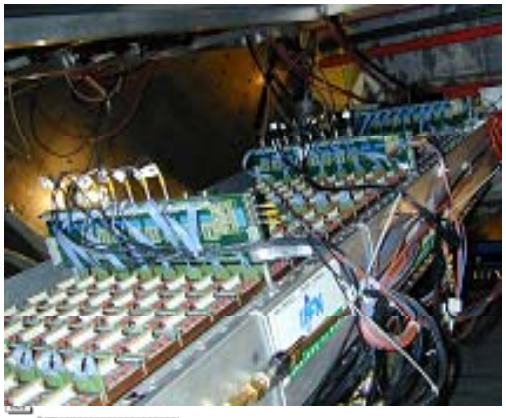
$$\sigma_x^2 = \frac{\sigma_{DRF}^2}{N_{p.e.}} + \sigma_g^2 + \sigma_e^2 + \sigma_f^2 + \sigma_{Corr}^2$$

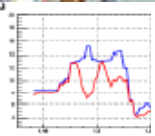
energy resolution plays only a secondary additional role when small volumes are involved

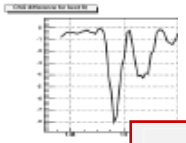
Θ^{++} Search



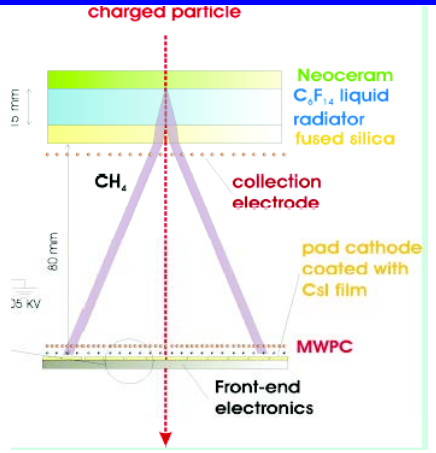
$$\frac{d\sigma}{d\Omega}(\gamma^* p \to \Theta^{++}K^-)\big|_{\theta=2^\circ} < 3nb$$

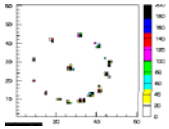






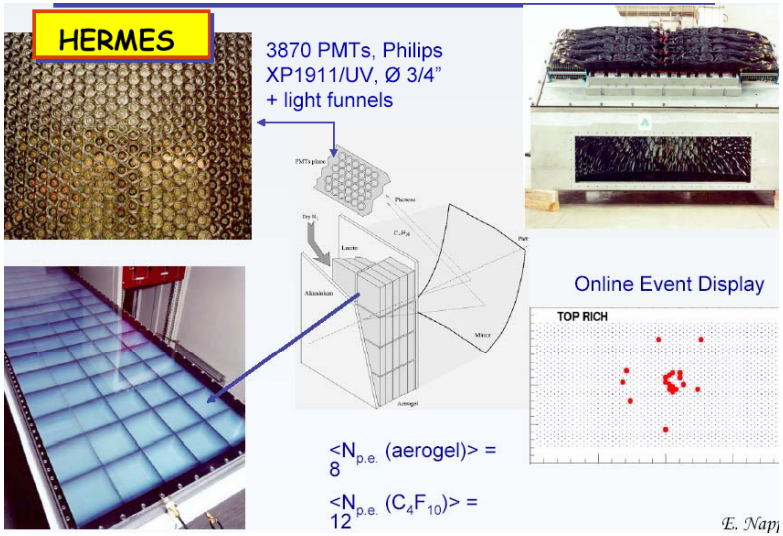
Freon/CsI RICH detector (like ALICE)



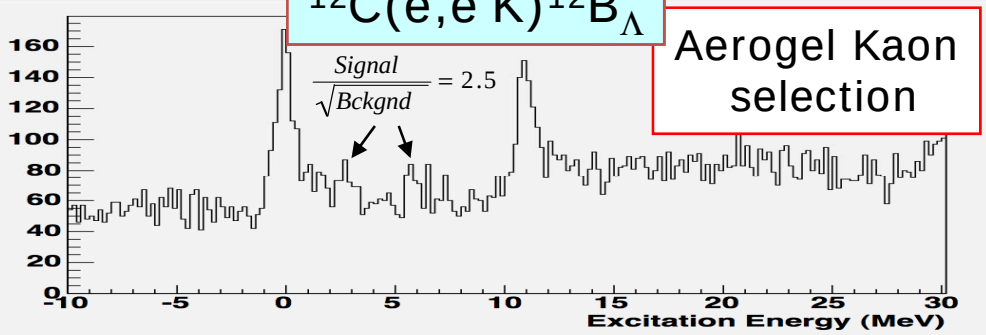


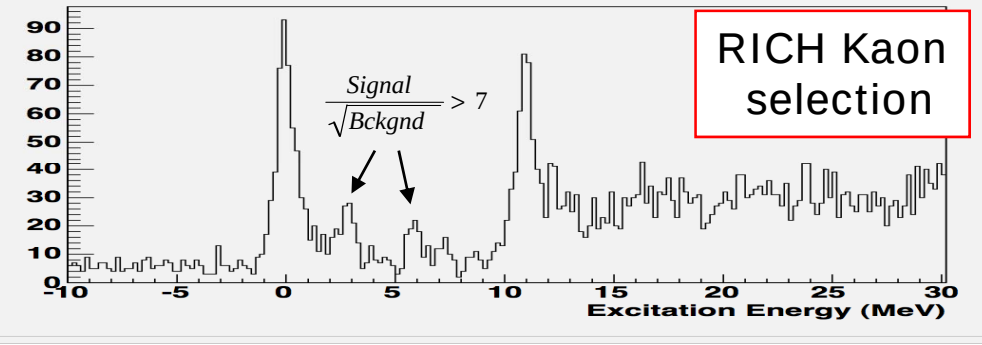
Spectroscopy analysis of $^{12}B_\Lambda$: Aerogel vs. RICH K-selection

Hermes areogel RICH



$^{12}C(e,e'K)^{12}B_\Lambda$





Full brick

Call :	FP7-HEALTH-2007-A
Funding Scheme :	CP Collaborative project
Proposal Number :	201620
Proposal Title :	Molecular Imaging Cardiac Repair with Stem Cells
Proposal Acronym :	MICARESTE
Stage :	1 of 1
Activity Code :	HEALTH-2007-1.2-4
Duration (month) :	60
Total project cost (€) :	16,886,665.00
EC funding requested (€) :	12,000,000.00

This proposal aims to elucidate the mechanism of action behind stem cell activity in cardiac regeneration, an area of tremendous contemporary pre-clinical and clinical activity. This ambitious proposal targets one of the most important questions arising in this field using a multiple way approach. The complex and innovative strategy to elucidate the mechanisms of stem cell mediated cardiac repair is highly valuable and could be beneficial for further development of pragmatic therapeutic strategies in this clinically relevant area. Such approach is complemented by the intention to develop multimodal molecular imaging technologies, primarily integrating SPECT with MRI. This technically difficult and challenging task would, if successfully accomplished, open new possibilities for the whole area of interest. Some aspects of this and other working tasks would, however, require more detailed clarification. Description of how novel MRI sequences, developed at high fields, will be translated to lower field clinical scanners is not given. It is also not clear how the data obtained in the pre-clinical phase can be translated to provide clinical benefit in humans, and what contingency plans exist for the planned work in case transplanted cells are quickly eliminated from the target tissue if they do not engraft. Progress beyond state-of-the-art is not clearly articulated, although the associated workplan is well organized.

2. Quality and efficiency of the implementation and the management

The proposal outlines sound management structures (including an advisory board) with a manageable number of partners and workpackages, albeit with a certain lack of mechanisms for conflict resolution. Consortium partners and leading figures are generally highly credible and devoted to their planned tasks. The consortium offers particularly significant strength in physical science, with less prominent expertise in biological and medical sciences. WP leaders are not identified in the application, and management activities at that level (as well as at the complex task level) are absent. The budget for instrumentation/equipment is reasonable; staffing budget is vague and lacks detailed specification. The overall budget is excessive, regarding the fact that the proposal aim is focused on the pre-clinical area, without extension to the clinical research.

- Appropriateness of the management structure and procedures
- Quality and relevant experience of the individual participants
- Quality of the consortium as a whole (including complementarity, balance)
- Appropriateness of the allocation and justification of the resources to be committed (budget, staff, equipment)

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HEALTH-2009-1.2-3

Novel MR-compatible PET detectors for simultaneous PET/MRI imaging

FP7-HEALTH-2009-single-stage

The focus should be to develop novel magnetic-field-compatible nuclear detectors for PET imaging, aimed at maximizing the benefits of simultaneous PET/MRI acquisition, which can also be used efficiently and implemented in stand alone PET or SPECT applications. These detectors should operate in high magnetic fields, as used in MRI, without performance degradation, and have high spatial and time resolution. A dedicated integrated readout of high quality should also be developed. The full detector should be compact so as to allow good integration with an MRI system. Globally, it should allow fully exploiting the advantages of both PET and MR technologies in a simultaneous imaging modality and for implementation in both preclinical and clinical/human PET stand-alone systems beyond the state-of-theart. Active participation of industry, especially SMEs, could lead to an increate impact of the research proposed, and this will be considered in the evaluation of the proposal. **Funding scheme:** Collaborative Project (Large scale integrating project).

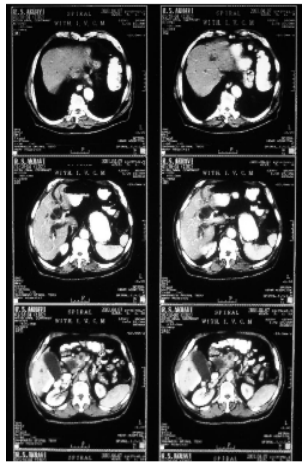
Participants in Large-scale integrating projects are required to conclude a consortium agreement

	1. Scientific and/or technological excellence *(relevant to the topics addressed by the call)* **(award)**	2. Quality and efficiency of the implementation and the management **(selection)**	3. The potential impact through the development, dissemination and use of project results **(award)**
All funding schemes	• *Soundness of concept, and quality of objectives*	• Appropriateness of the management structure and procedures • Quality and relevant experience of the individual participants	• *Contribution, at the European [and/or international] level, to the expected impacts listed in the work programme under relevant topic/activity*
Collaborative projects	• *Progress beyond the state-of-the-art* • Quality and effectiveness of the S/T methodology and associated work plan	• Quality of the consortium as a whole (including complementarity, balance) • Appropriateness of the allocation and justification of the resources to be committed (budget, staff, equipment)	• Appropriateness of measures for the dissemination and/or exploitation of project results, and management of intellectual property.

EC contribution

€ 12 million

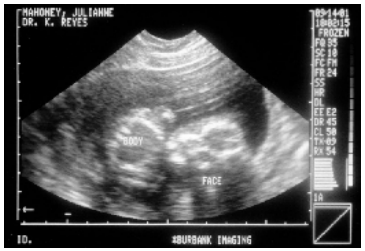
Molecular Imaging Modalities



CT

A Tissue Density, Z
20-50 µm

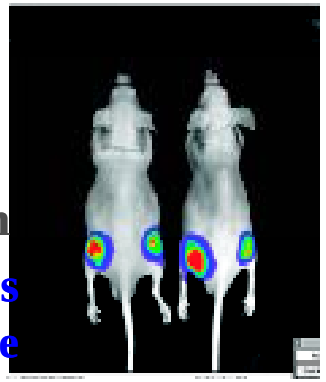
Ultrasound



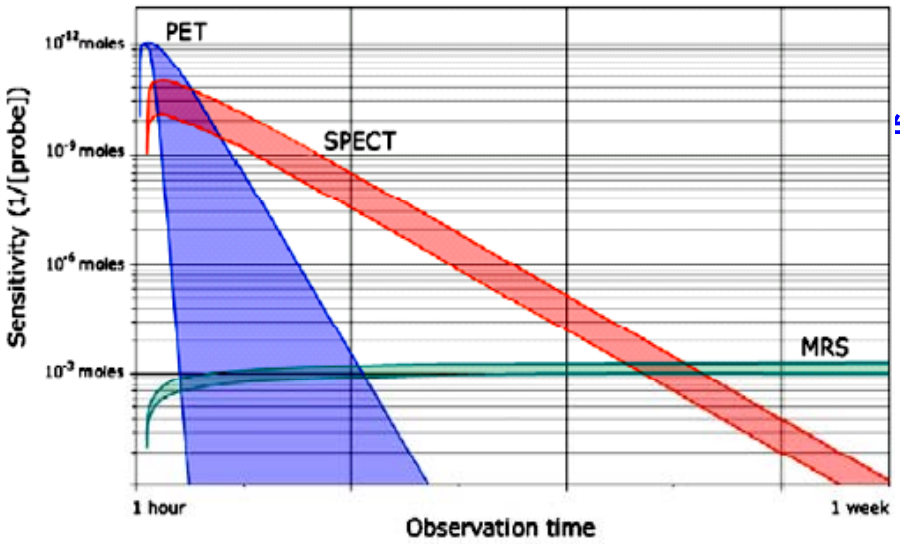
A F
Structure
0.1 mm
Doppler

Optical
(Bioluminescence, fluorescence)

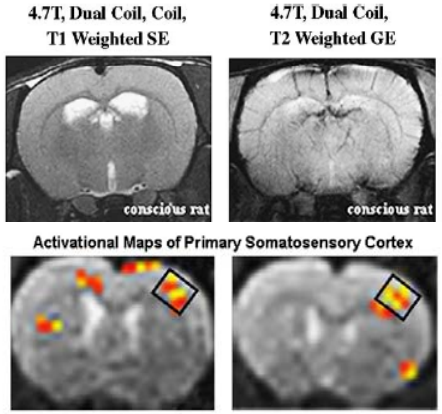
A M
Topography
µm to mm
~10^3 cells
= quantitative



Unique !!



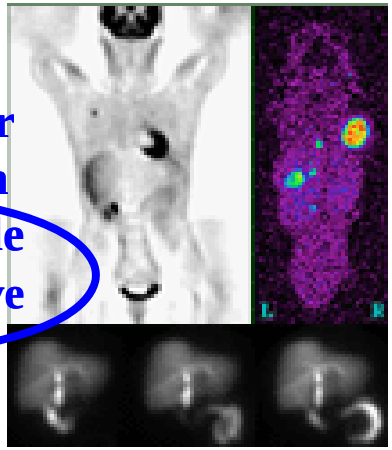
MRI



A F M
H Concentration
0.1 mm
BOLD, DCE
β-galactocidase
0.1 µmole H / µmole ^{31}P

PET/SPECT

F M
Radiotracer
~1-2 mm
<10^{-12} mole
= quantitative



what we shoudl do to be successfull ?

- loking at applications (“added value” by combining the modalities)

- good (new???) detectors

- “perfect” integration in multimodality (hardware and software)

- PET/SPECT

high field and low field

- “smart layout (s)”

- TOF – PET → scintillator, electronics, sensor

- What to propose ?

- Management and careful writing of the proposal (only 1/3 of the evaluation is on “technical/scientific)!!

What we have to study → design

PET-SPECT MRI

Low field

High field

What we have to build

- a prototype of SPECT/PET – MRI (high field) for

- brain
- heart

- a prototype of SPECT/PET – MRI (low field) for

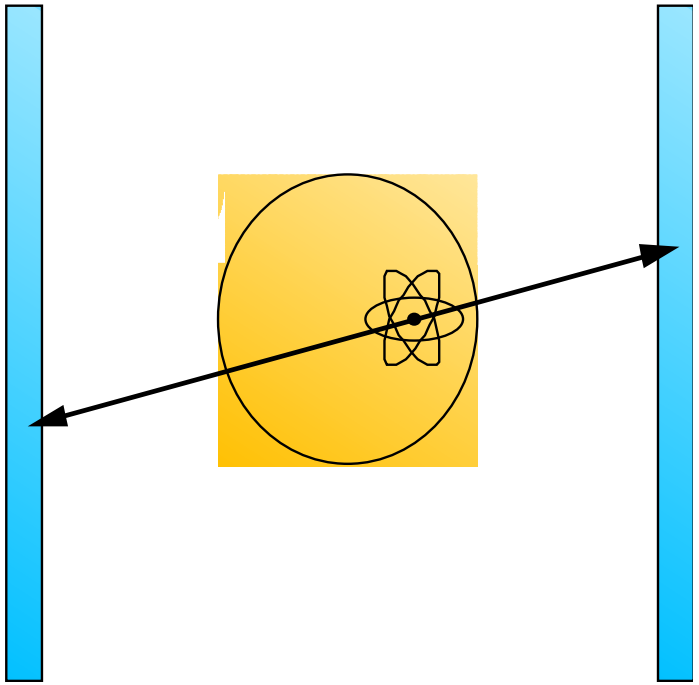
- breast
- small animal

Com
Simult
T

Abstract—Parkinson's disease (PD) is a widespread neurodegenerative disorder characterized primarily by changes in motor function. It affects the dopamine transporter (DAT) system, and results in a reduction of DAT specific binding and volume of active dopamine transporters, in the striata. Early detection of PD, before the onset of clinical symptoms, has great potential in improving patient management. Dual-isotope SPECT allows the assessment of different brain functions under identical physiological conditions. Simultaneous dual-isotope studies have a further advantage over sequential studies as they provide perfect image registration and reduce imaging time for the same total collected counts. These advantages are limited however by cross-talk and downscatter between the two isotopes, especially in the case of ^{123}I and ^{99m}Tc where the emission energies are very close (i.e., 159 and 140 keV). We compare DAT brain PET with sequential and simultaneous pre- and post-synaptic dual-isotope SPECT for the task of estimating striatal activity concentration and striatal size for a normal brain and for three early stages of PD. We used the Cramer-Rao lower bound, representing the theoretical best performance achievable, as our performance metric to objectively compare these modalities, and determine their performance in identifying early disease stages. Our findings show that PET and simultaneous and sequential SPECT can successfully identify the early stages of PD when estimating both pre-synaptic activity concentration and size. Post-synaptic SPECT imaging was not able to separate disease stages. PET and simultaneous SPECT perform well when estimating only activity concentration or size, but sequential SPECT has significantly degraded performance due to lower statistics.

Dual Modality: PET / SPECT

(Use SPECT Camera for PET)



- **SPECT cameras optimized to image 140 keV (not 511 keV) photons.**
- **Detectors are “thin” (0.8 attenuation lengths) NaI:Tl.**
  - **⇒ lower efficiency**
  - **⇒ higher scatter fraction**
- **Large gaps in angular coverage**
  - **⇒ rotate for complete sampling**
  - **⇒ lower solid angle coverage.**
- **Detector area**
  - **⇒ large dead time effects**

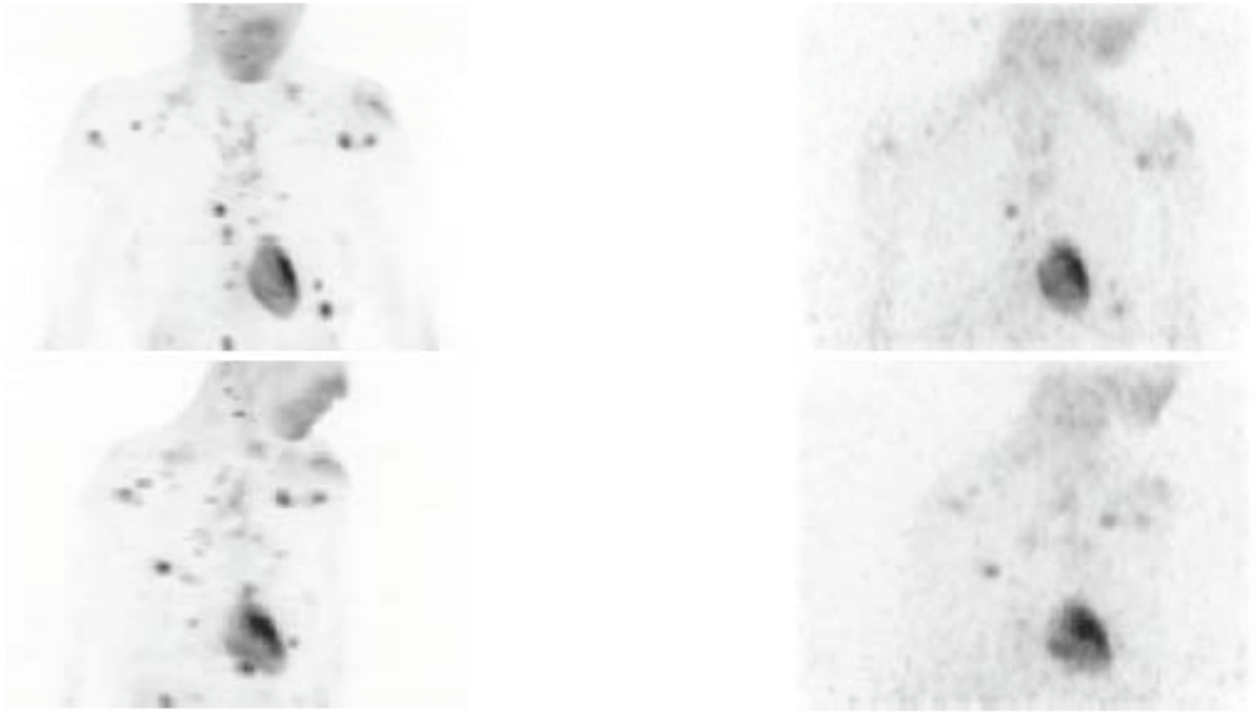
Old slide from B. Moses

Less Expensive, But Not Optimized for PET

The Big Question:

PE- PET / SPECT Performance is Inferior to PET, but

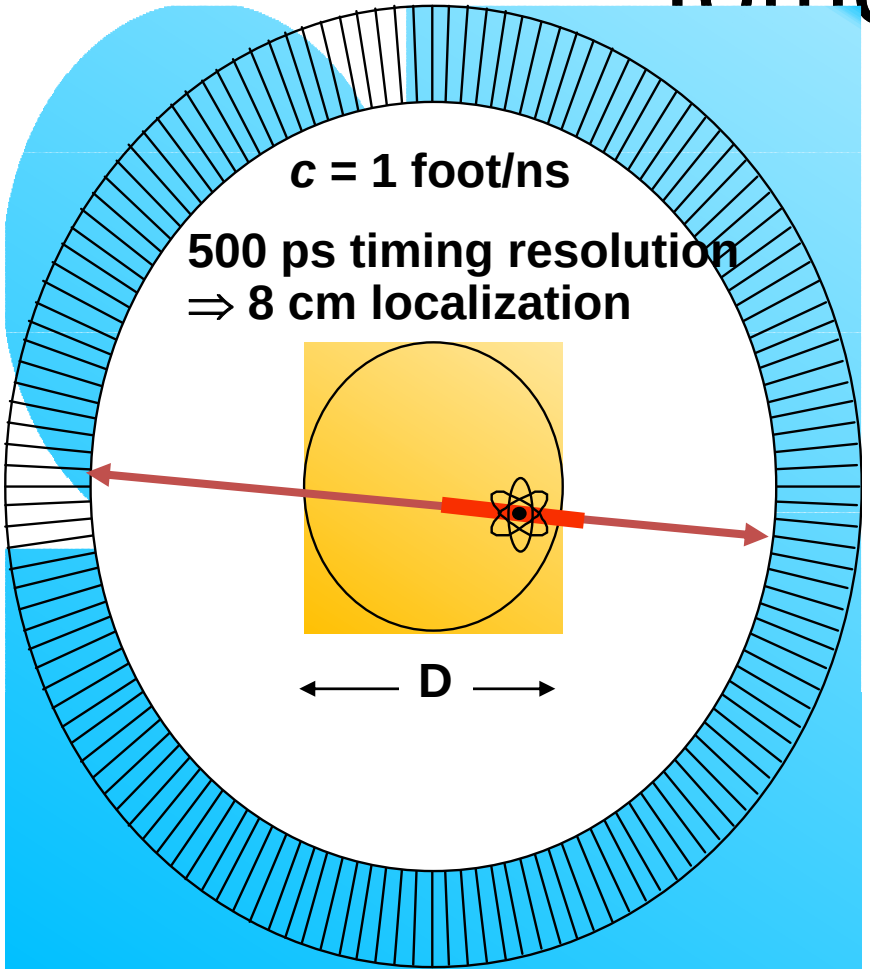
Dedicated PET **PET / SPECT**



*Data courtesy of Tom Lewellen, University of Washington

Is It Clinically Useful???

Time-of-Flight Tomograph



- **Can localize source along line of flight.**
- **Time of flight information reduces noise in images.**
- **Time of flight tomographs have been built with BaF_2 and CsF.**
- **Difficult to keep all detectors in accurate time coincidence.**
- These scintillators force other tradeoffs that reduce performance.

Not Compelling with Present Technology…

Old slide from B. Moses

- **Variance Reduction Given by $2D/c\Delta t$**
- **500 ps Timing Resolution ⇒ 5x Reduction in Variance!**

Characterizatic T Scanner

Benefit of Time-of-Flight in PET: Experimental and Clinical Results Joel S. Karp, Suleman Surti, Margaret E. Daube-Witherspoon, and Gerd Muehllehner Department of Radiology, School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

SUMMARY

We have developed a proto-type whole-body TOF scanner based on lanthanum bromide that is fully 3D and has an axial FOV of 25 cm. The system is currently operating in a laboratory environment. Thus, it does not yet have gantry covers or a patient bed, so have only performed phantom measurements to date. We will, however, complete the system

resolution are achieved in addition to excellent energy resolution and timing resolution. To date, we have measured an overall system energy resolution of 7.5% fwhm and a

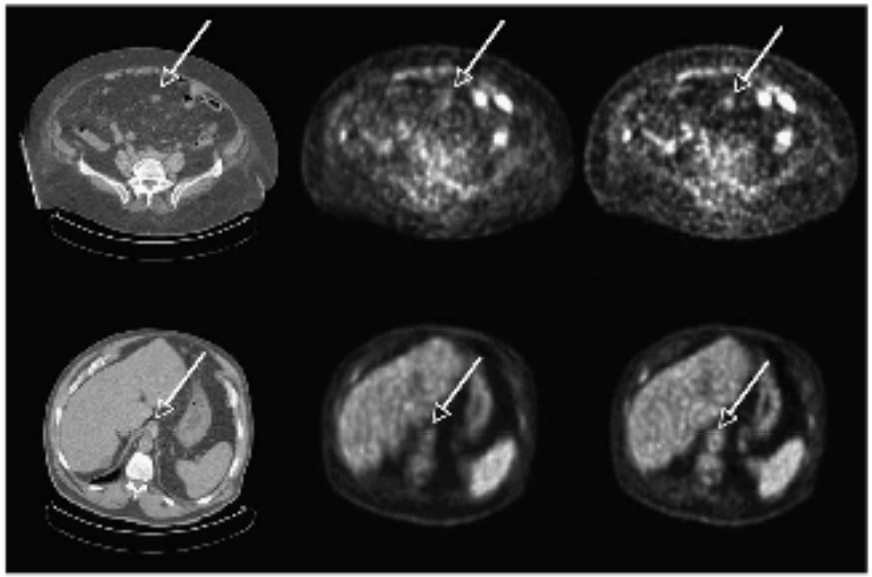


FIGURE 3. Representative transverse sections of 2 different patients: low dose CT (left), non-TOF MLEM (middle), and TOF MLEM (right). (Top) Patient 1 with colon cancer (119 kg, BMI = 46.5) shows a lesion in abdomen seen in CT much more clearly in TOF image than in non-TOF image. (Bottom) Patient 2 with abdominal cancer (115 kg, BMI = 38) shows structure in the aorta seen in CT much more clearly in TOF image than in non-TOF image.

reconstruction reaches convergence faster than the non-TOF reconstruction, and the rate of convergence is seen to be more insensitive to object size. These results indicate that TOF will help improve image quality and potentially reduce scan time with clinical patients.

Time-of-Flight and SNR

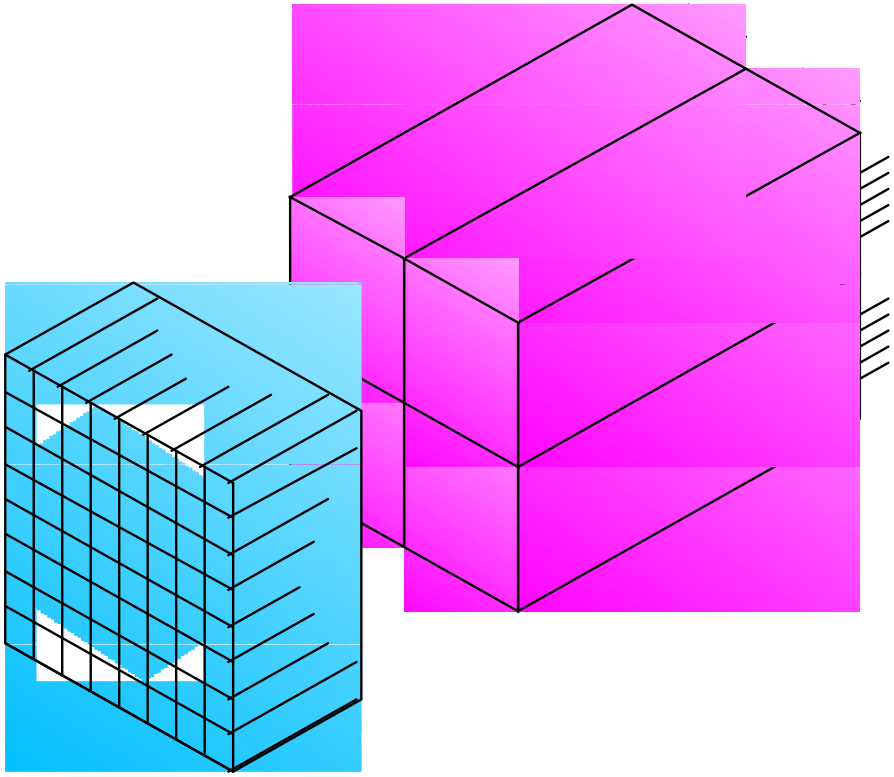
$$\Delta x = \frac{\Delta t}{2} c$$

$$SNR_{TOF} \cong \sqrt{\frac{D}{\Delta x}} \cdot SNR_{conv}$$

Time Resolution (ns)	Δx (cm)	SNR improvement (20 cm object)	SNR improvement (40 cm object)
0.1	1.5	3.7	5.2
0.3	4.5	2.1	3.0
0.5	7.5	1.6	2.3
1.2	18.0	1.1	1.5

- Patient port ~60 cm diameter 24 to 48 layers, covering 15 cm axially.
- 4-5 mm fwhm spatial resolution.
- ~2% solid angle coverage
- $1 – $2 million dollars.

Detector Requirements



Detect 511 keV Photons With (in order of importance):

- >85% efficiency
- <5 mm spatial resolution
- “low” cost (<$100 / cm^2)
- “low” dead time (<1 μs cm^2)
- <5 ns fwhm timing resolution
- <100 keV energy resolution

Based on Current PET Detector Modules

IOP PUBLI
Phys. Med.
AND BIOLOGY
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Effec
on pl
emiss
ctors

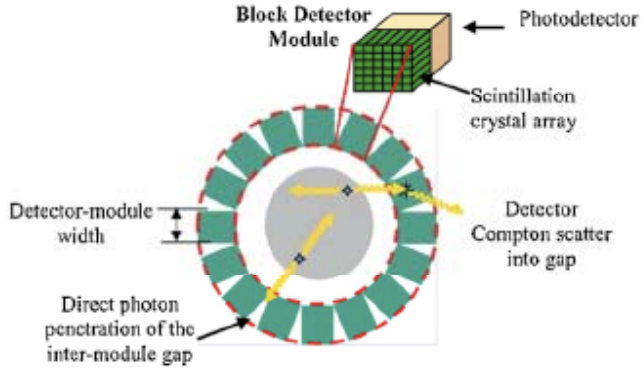

Figure 1. Rectangular block detectors formed into a cylindrical system configuration produce a significant number of inter-module wedge-shaped gaps that provide a path for Compton-scattered photons in the detectors to escape.

F Habte[1], A M K Foudray[2,3], P D Olcott[2] and C S Levin[2]

[1] Nuclear Science and Technology Division, Oak Ridge National Laboratory, Oak Ridge, TN 37831-6010, USA
[2] Department of Radiology, Stanford University, 300 Pasteur Dr, Stanford, CA 94305-5128, USA

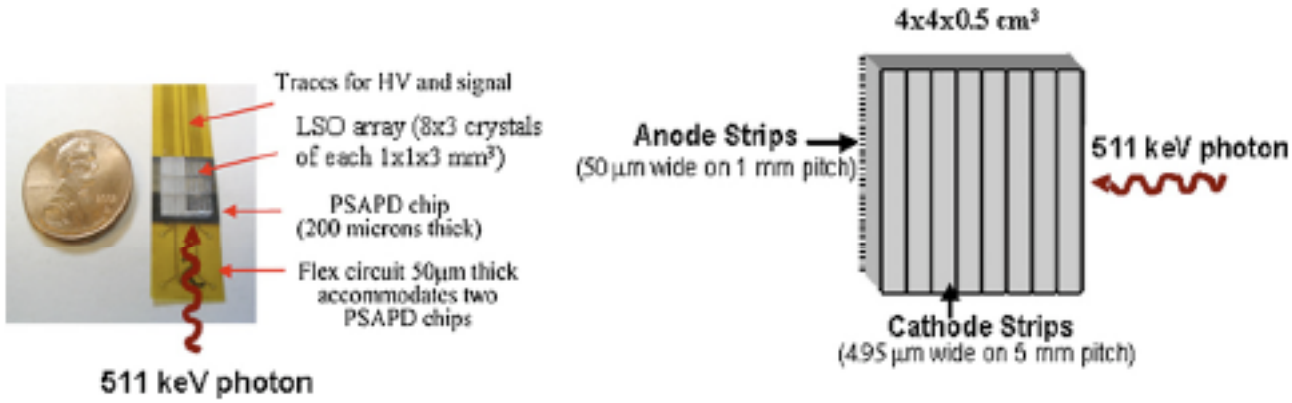

Figure 2. 1 mm resolution detector technologies under study. Left: LSO-PSAPD; right: cross-strip cadmium zinc telluride (CZT).

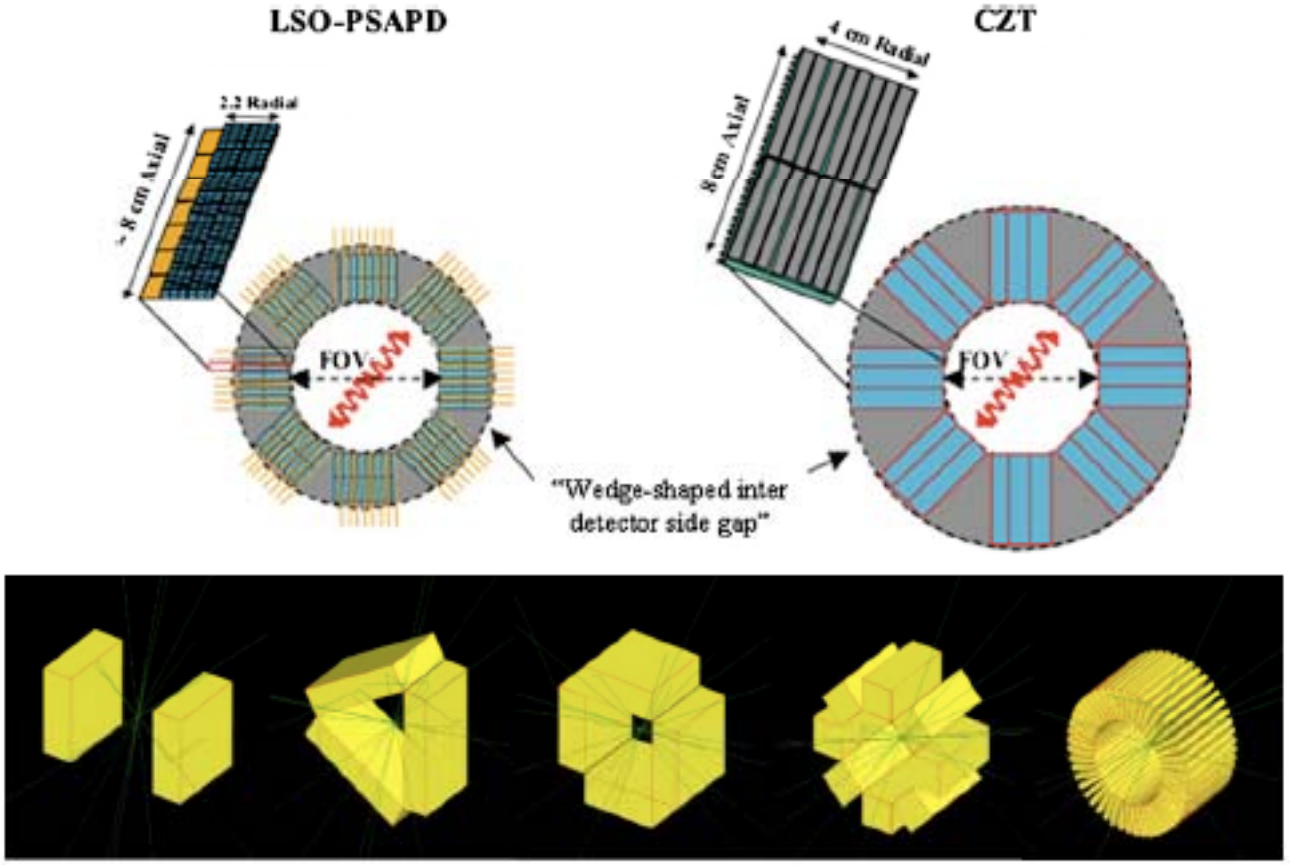

Figure 4. Different detector configurations using 2-, 3-, 4-, 8- and 48-sided detector system 'polygons' forming a fixed 8 cm transaxial and 8 cm axial FOV. The rays shown traversing the detectors indicate example photon tracks through the detector system.

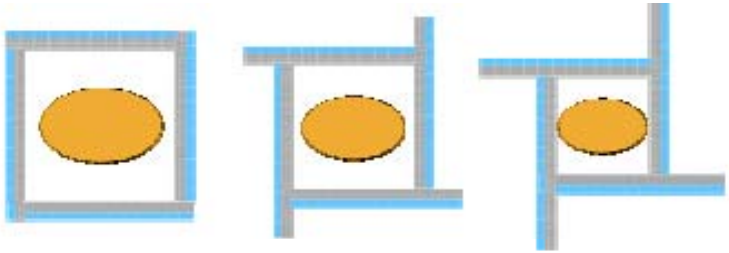

Figure 8. Proposed variable FOV rectangular clinical whole-body PET system. Left: 63 × 63 × 16 cm^3 FOV, middle: 53 × 53 × 16 cm^3 FOV, and right: 41 ×41 × 16 cm^3 FOV. The axial FOV is fixed at 16 cm.

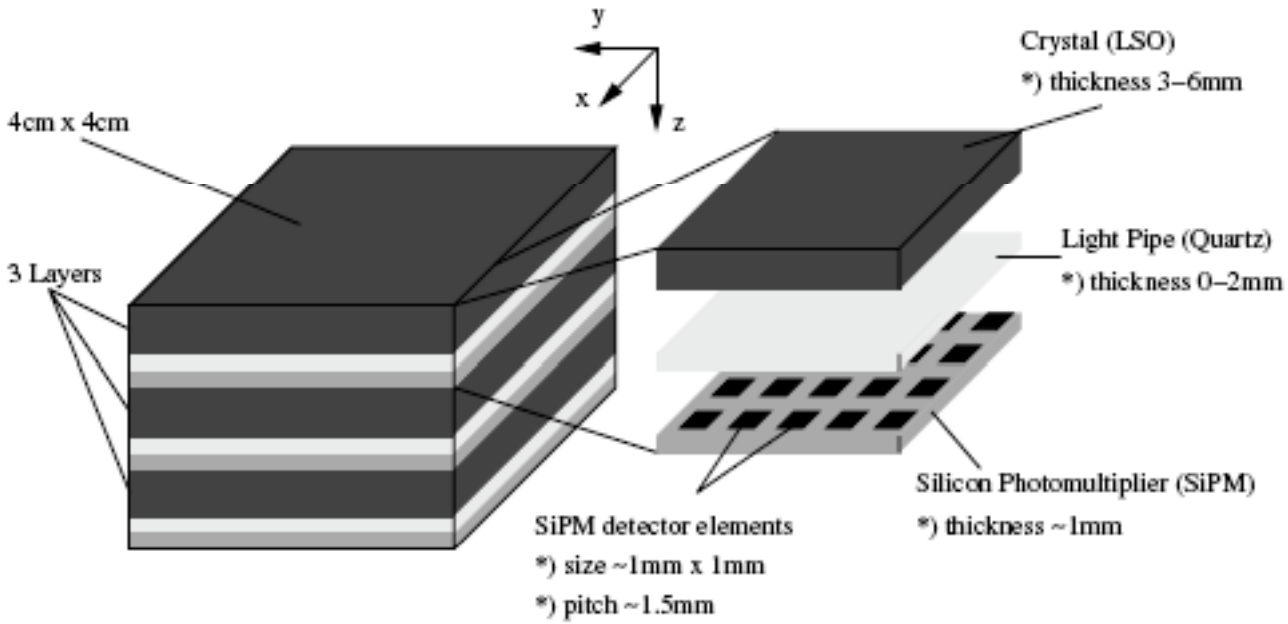

Figure 1. A single detector head consisting of three module layers on the left and an exploded view of a module layer on the right showing the pixellated silicon photomultiplier (SiPM).

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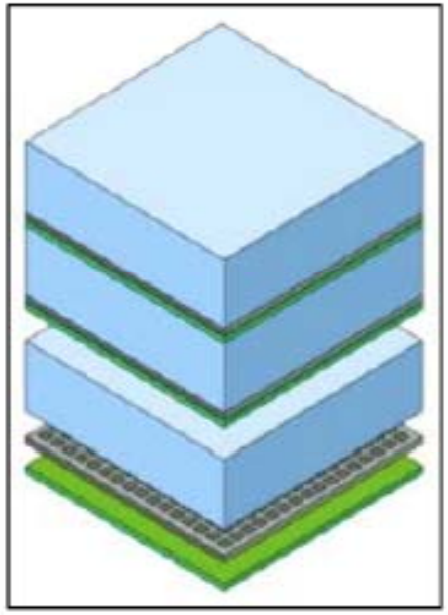
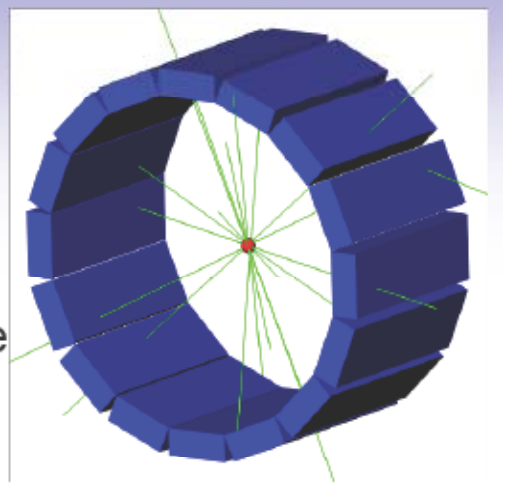
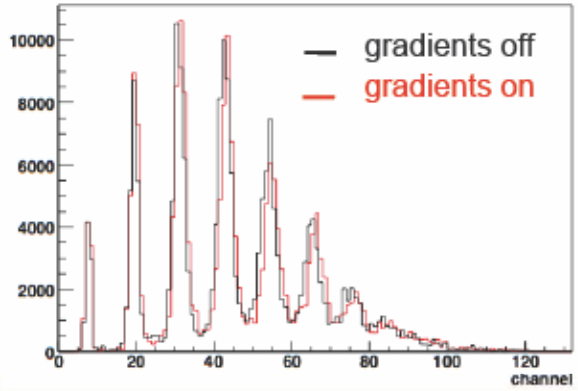


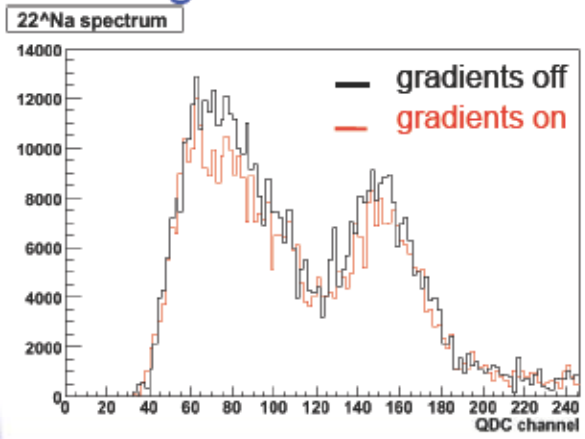
MR compatible ring tomograph

- Ring tomograph to be inserted in a magnet bore of an MR system.
- 16 detector heads, 7 cm x 2.4 cm;
- FOV axial 7 cm, transaxial FOV ~6 cm.
- Spatial resolution: 0.76 mm^3 for a ^{18}F point source in the CFOV with FBP.
- efficiency around 11% for 250 keV energy threshold.



Tests with SiPMs in MR system show no degradation of the data

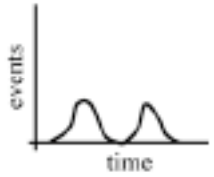




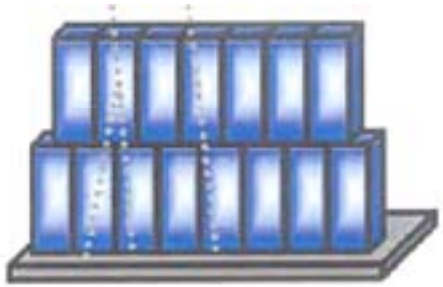
DOI mandatory

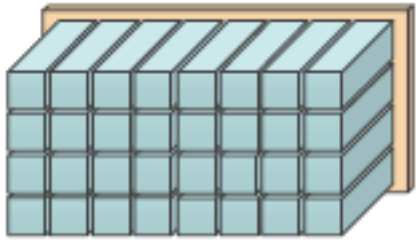
Two or more layers of scintillators that have different decay times.

Use PSD to identify which crystal is the site of interaction.



Some scintillator combinations that have been used:
LSO/LSO
NaI(Tl)/LSO
BGO/GSO
GSO/LSO/BGO/CsI(Tl)





SPECT/PET

- mixed ring, "trivial"
- full ring

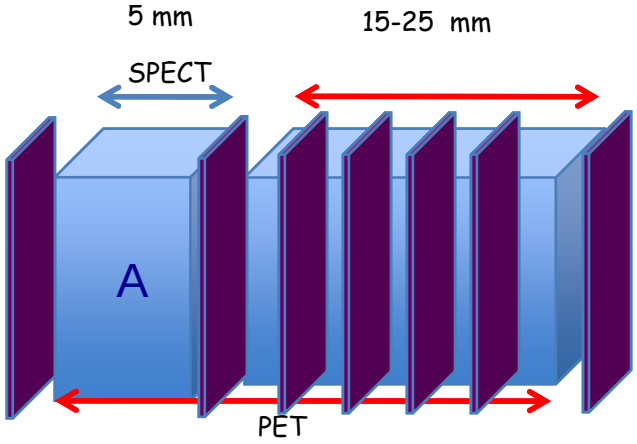
  - at the same time? → reducing too much the sensitivity
  - consecutively? How to build this?

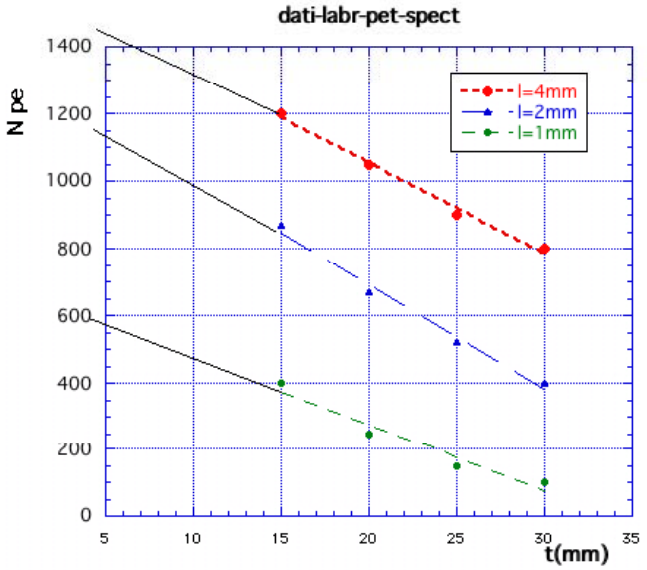
Scintillator → LaBr3

- fast
- light yield

but

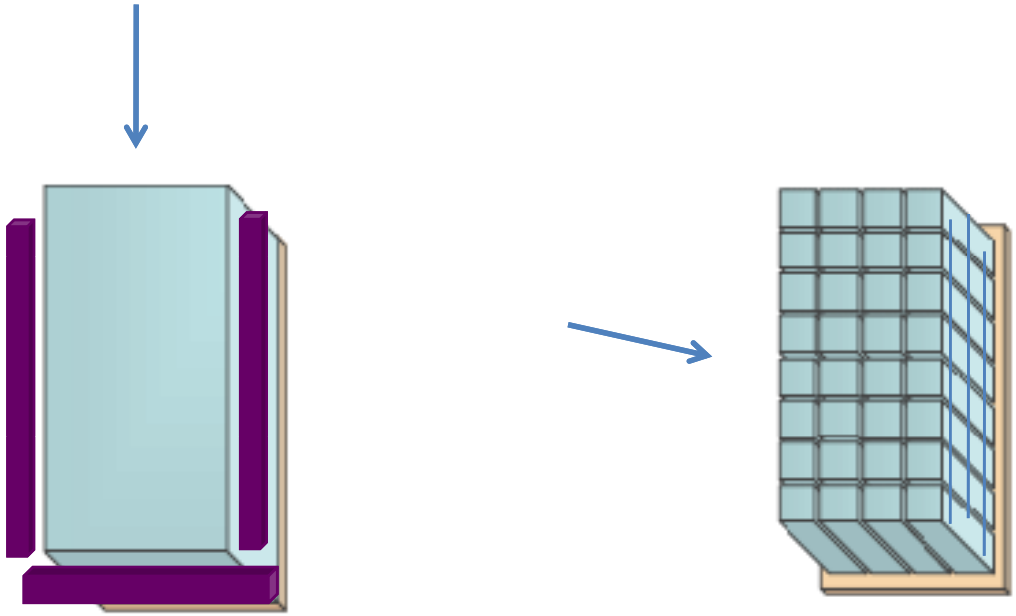
- hygroscopic





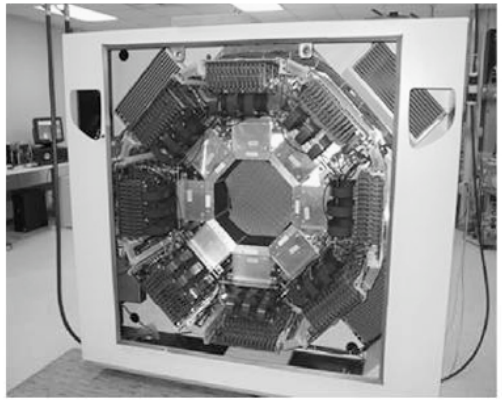
Different layout possible for A and B

- continuous single slice (for Pet) or several slices (with equal or increasi
- pixellated
  - modules of 50 x 50 x 20 (30) mm3 with pixels 2 x2 or 3 x3 or 4 x 4 mm2 (problems with DOI)
  - same scheme
  - modules of 50 x 50 mm2 with pixel "cubes" of 2 x2 x2 mm3 (or 3 x 3 x 3 mm3) (brute force) (diverging number of channels?)



brain

- 6 sides (at least) to be "small" and compatible with the SPECT layout (FOV > 20 x 20 cm2



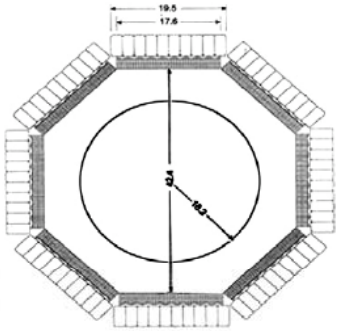
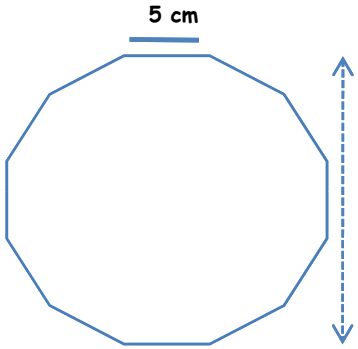


Fig. 3. The HRRT and its layout.

Small animal (and breast)



25 -30 cm