Novel design of a parallax-free Compton enhanced PET camera module:

Towards high-resolution functional brain imaging

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Introduction

- CERN and the LHC - Scintillators, photodetectors, electronics …
- Technology transfer from HEP to Medical Imaging

Positron Emission Tomography

- Principle and intrinsic limitations
- State of the art

Hybrid Photon Detectors: Principle, performance and fabrication

The 3D axial PET camera

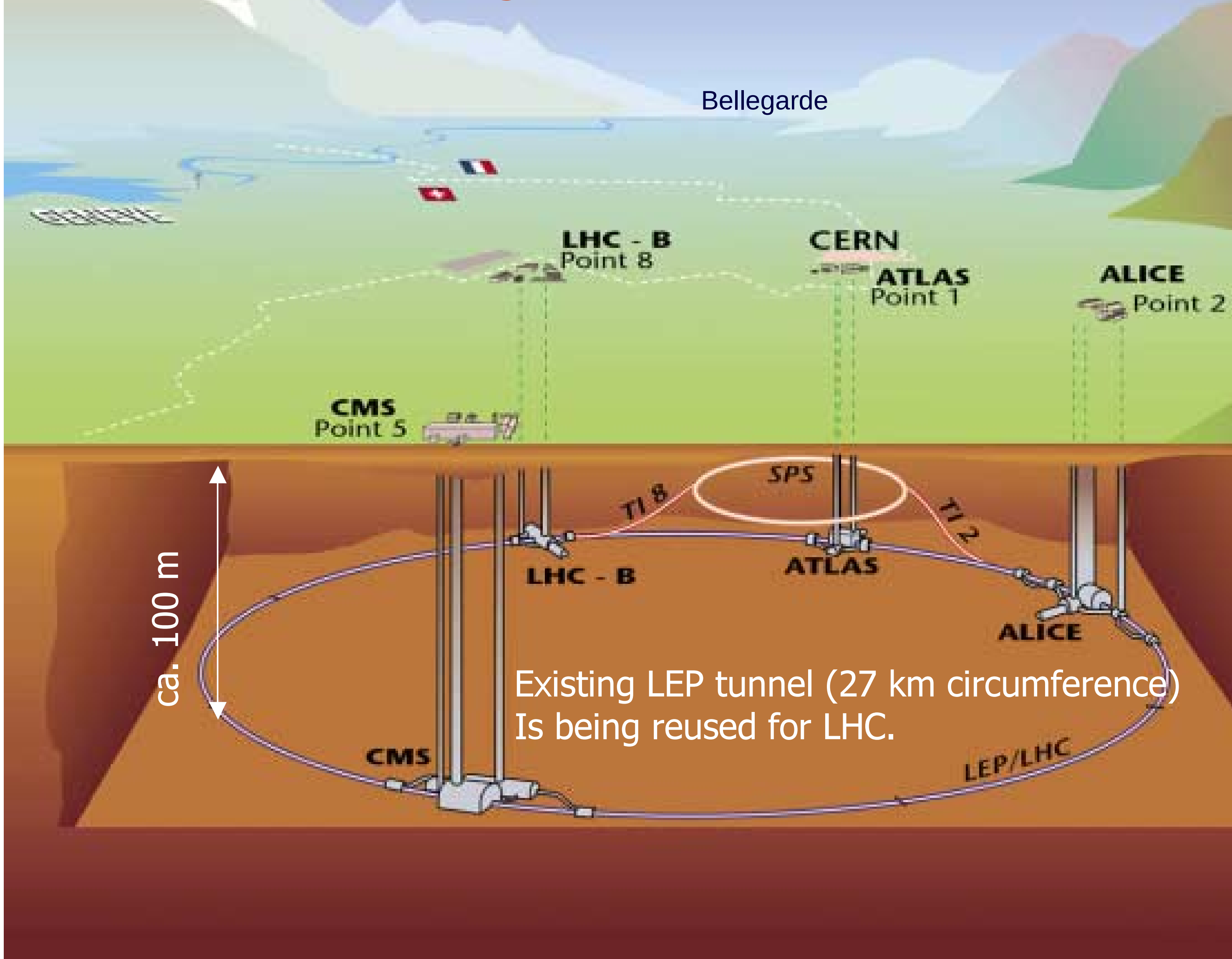
- concept
- strong and critical points
- discussion of the key components
  (scintillator, photo detector, electronics, integration)
- Brain PET study: geometry and first performance estimates

EuroMedIm

- philosophy
- the collaboration
- the projects


Jura
Lac Léman
CERN - Prévessin
airport
CERN - Meyrin

LHC - The Large Hadron Collider



LHC

p-p collisions
at 14 TeV (10^{12} eV)

Pb-Pb collisions at
1312 TeV

~ 5000
superconductive
magnets (T=1.9 K)

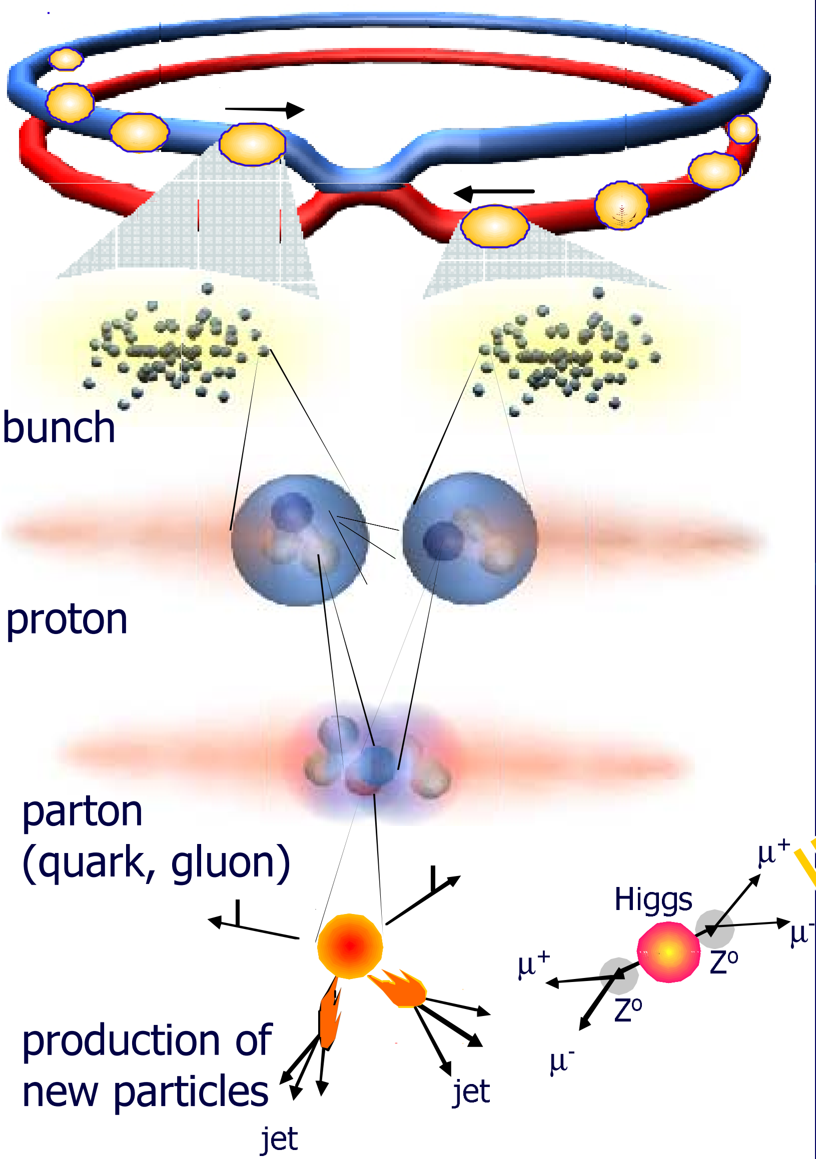
luminosity:
10^{34} cm^{-2} s^{-1} (pp)
10^{27} cm^{-2} s^{-1} (Pb-Pb)

4 large experiments

~ 10.000 people
involved

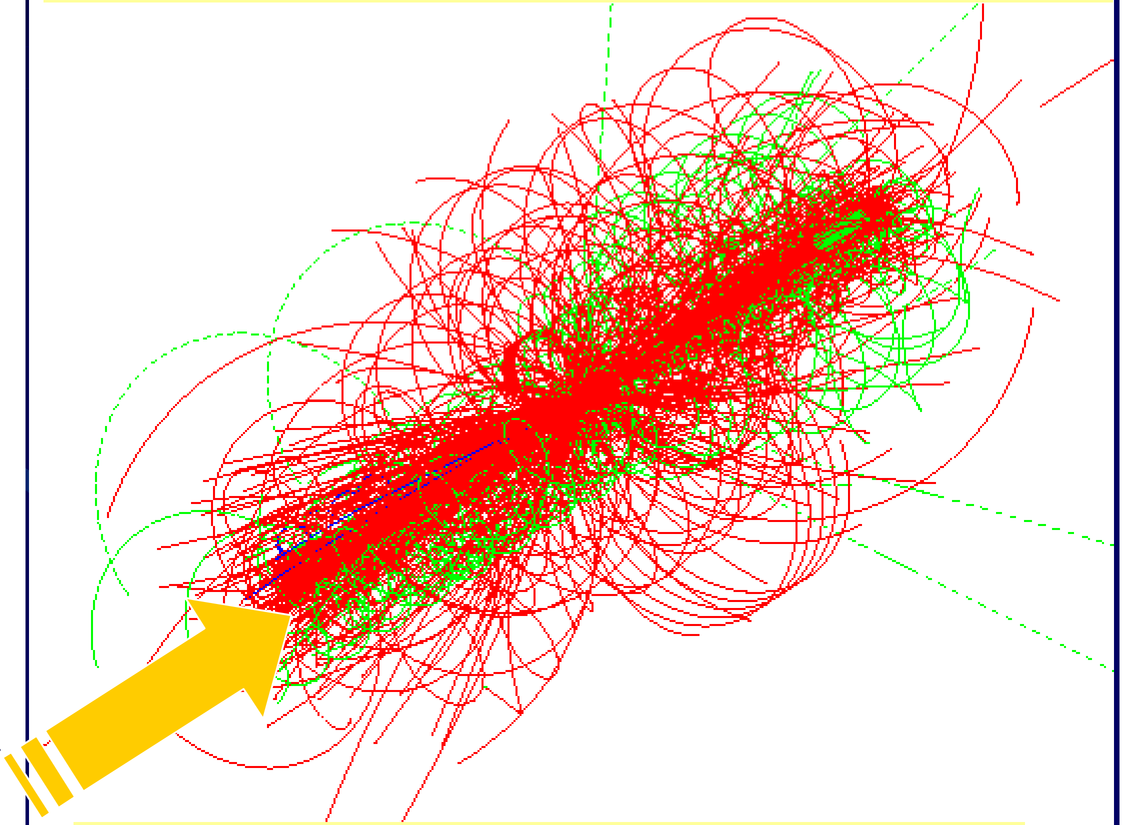
Start-up: 2007

What happens when… ?



The LHC bunch crossing rate is 40 MHz

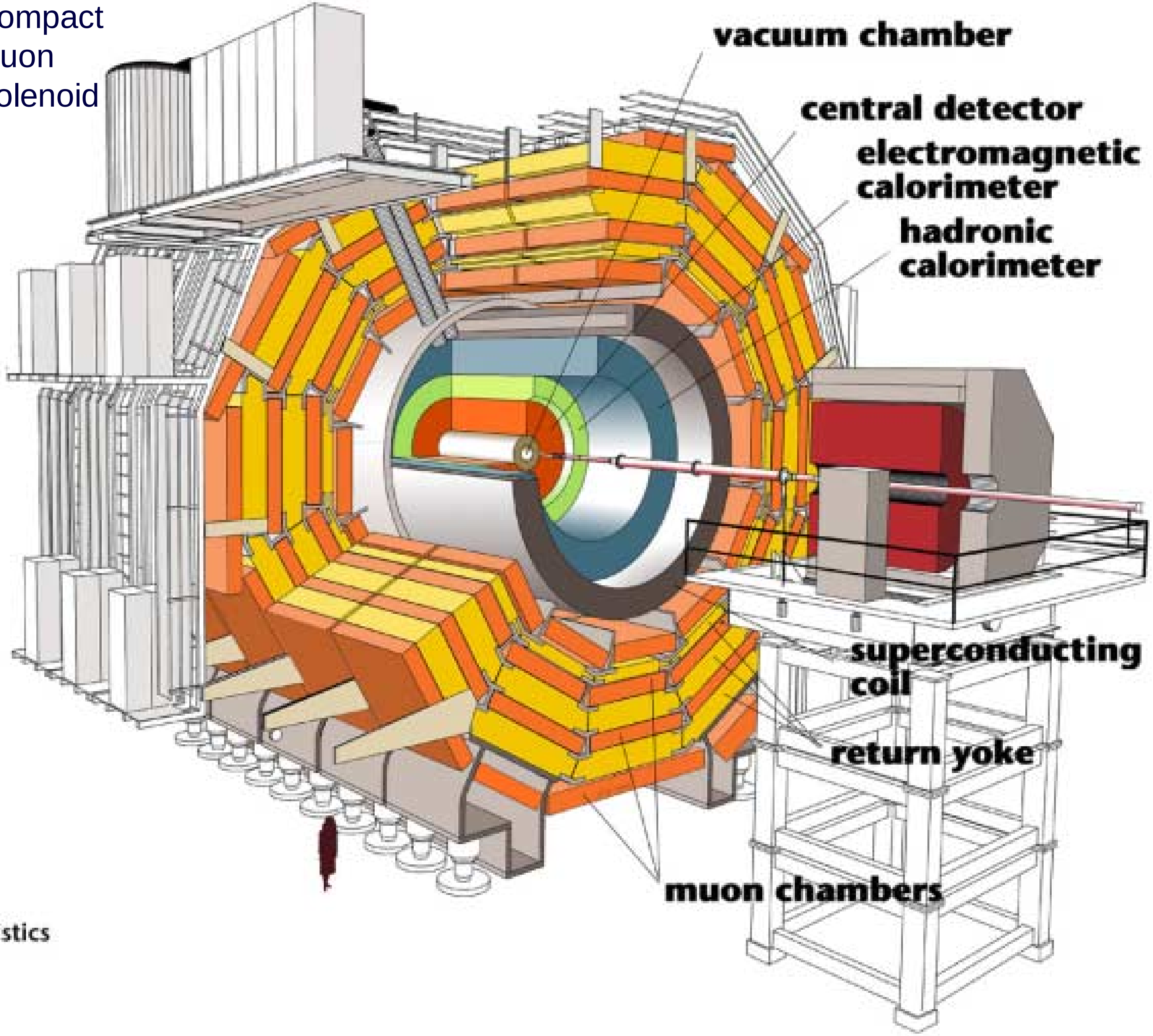
~ 20 reactions / crossing and 4000 particles produced



Expected rate of "New physics" (Higgs, SUSY,…)
0.00001 Hz

Required event selection: 10^{-14} !

Compact
Muon
Solenoid



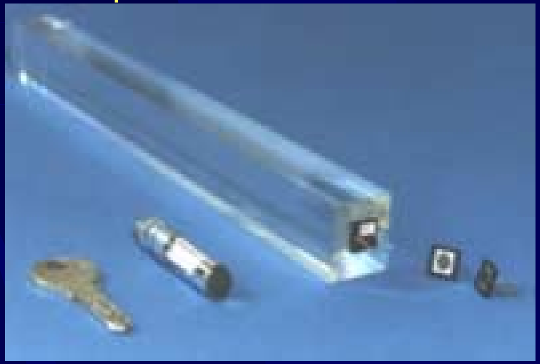
Detector characteristics

Width: 22m
Diameter: 15m
Weight: 14'500t

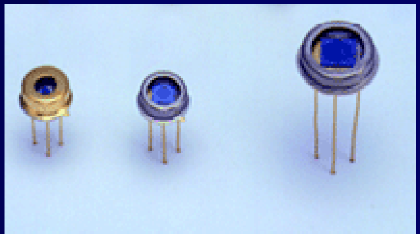
Which technologies can be transferred to medicine ?

- Scintillation crystals
- Photo Detectors
- Electronics (Front-end + Trigger)
- Simulation software
- …

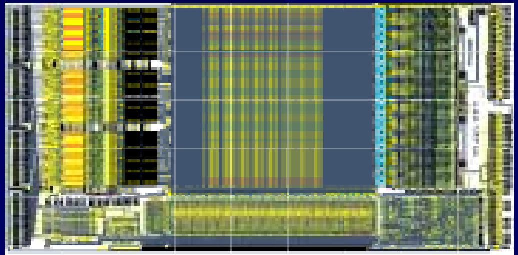
$PbWO_4$ crystals developed for the CMS experiment



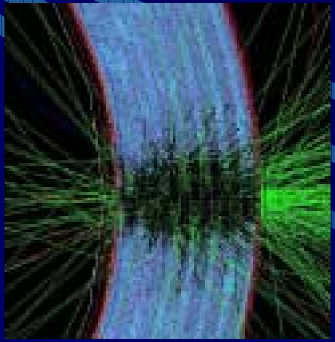
Avalanche Photo Diodes (APD)



Electronics chips + boards



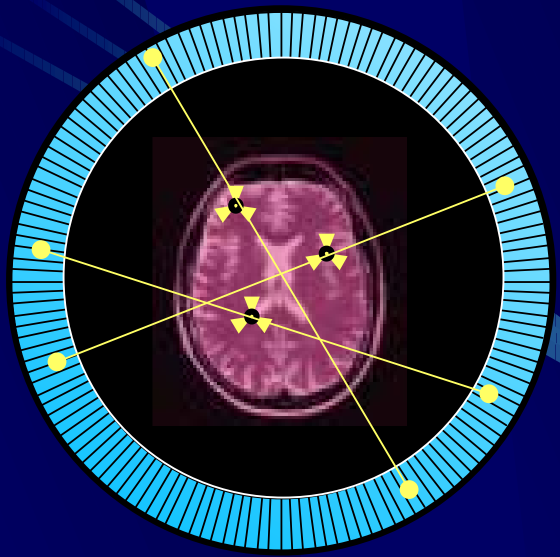
Hybrid Photon Detectors (HPD)



Geant4 simulation of ATLAS calorimeter

Positron Emission Tomography

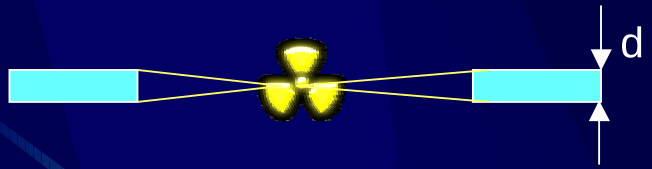
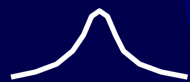
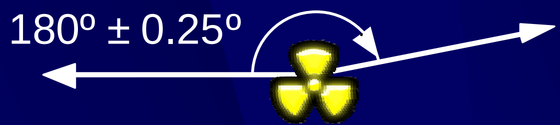
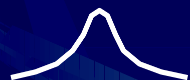
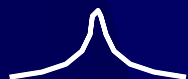
Principle and fundamental limits



Standard PET geometry

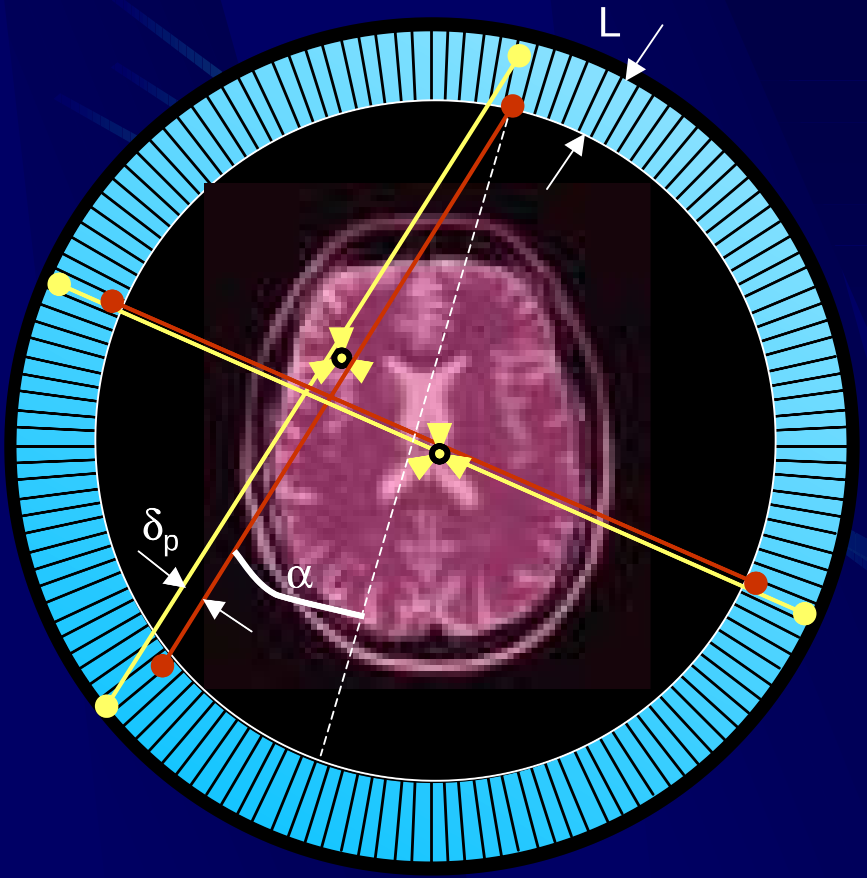
- Patient injected with positron (β^+) emitting radiopharmaceutical , e.g. FDG, marked with ^{18}F.
- β^+ annihilates with e^- from tissue, forming an annihilation photon pair (back-to-back, 511 keV)
- 511 keV pairs detected in scintillator crystals via time coincidence
- β^+ emission point lies on line defined by detector pair (line of record LOR, chord)

- Reconstruct 2D image using Computed Tomography
- Use stacked detector rings to obtain a 3D volumetric image.
- + many mathematical tricks (filtering, density corrections, …)

Factor	Shape	Resolution (FWHM)
 Detector Crystal Width		d/2
 Anger Logic		0 (individual coupling) 2.2 mm (Anger logic, empirically)
 Photon non-collinearity		1.8 mm (depends on det. ring radius)
 Positron range		0.5 mm, ^{18}F 4.5 mm, ^{82}Rb
Reconstruction Algorithm	multiplicative factor	1.25 (in-plane) 1.0 (axial)

Courtesy of B. Moses, Mattinata 2002

The parallax dilemma



Standard PET geometry

- Crystals need to have a minimum thickness L

  Efficiency for pair detection $\varepsilon_2 = \left(1 - e^{-L/\lambda_a}\right)^2$

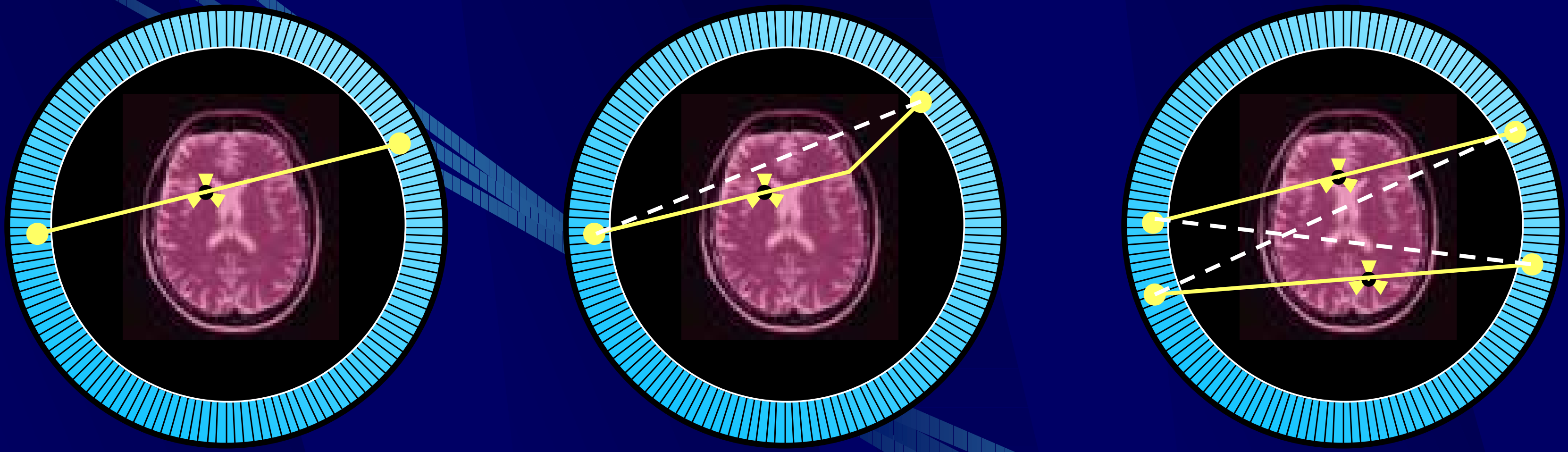
  λ_a = photon attenuation length of crystal
  L = λ_a → ε_2 ~ 40%, L = 2 λ_a → ε_2 ~ 75%, …
  λ_a = 1-2 cm (depending on material, see below)

- A standard PET does not measure the depth of interaction (DOI) in the crystal.
- This introduces a parallax error $\delta_p = L \cdot \sin\alpha$
- The resolution in the off-center region degrades significantly
- Solution: reduce L (→bad ε_2) or measure DOI or invent a different geometry

Resolution is important, but also sensitivity and image quality matter !

Sensitivity = True Event Rate / µCi / cm^3 (measures detector efficiency)

Determined by geometry, choice of scintillator, data acquisition…



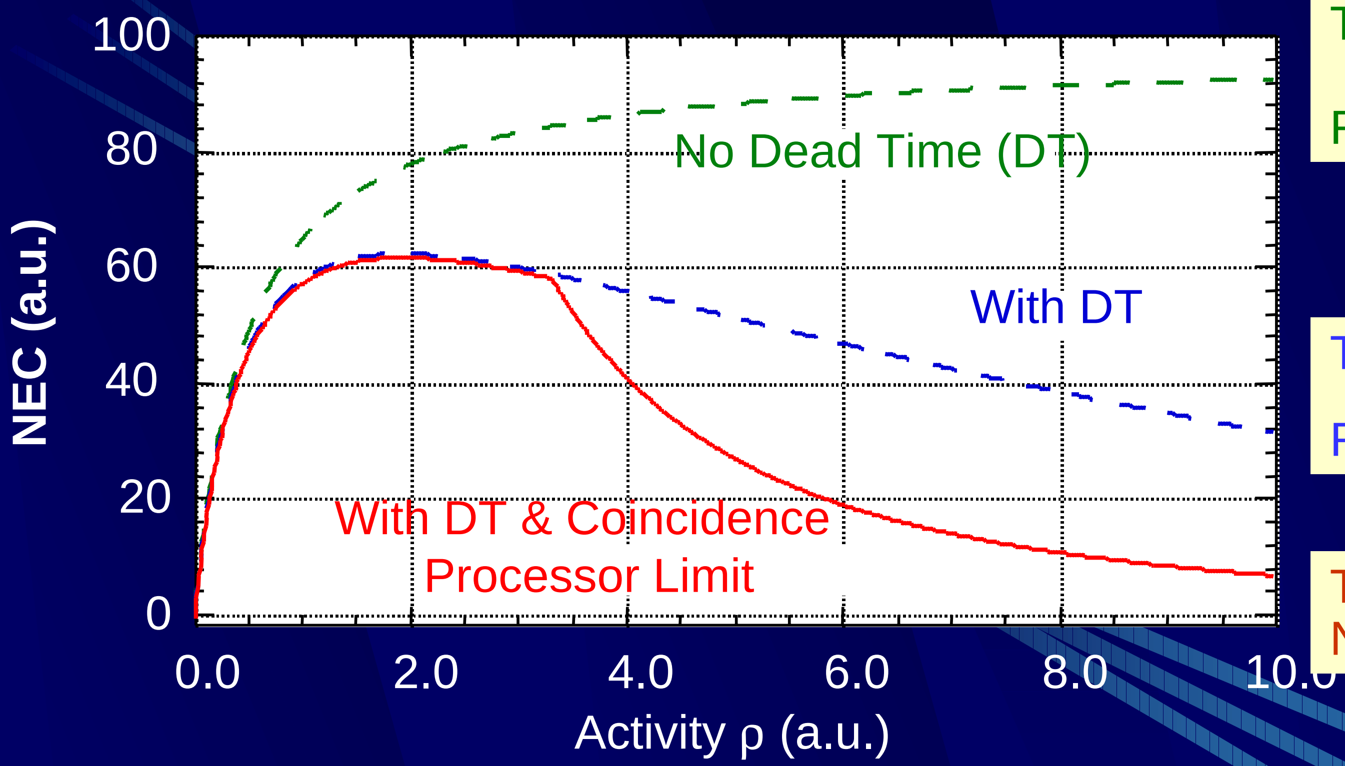
Trues Scatters Randoms

But the signal is subject to background from Compton scattering and random coincidences.

Noise Equivalent Count Rate

$$NEC = \frac{T^2}{T + S + 2R} \approx Signal \cdot \frac{Signal}{Background}$$

The NEC rate depends on many factors.



$T \propto \rho$, $R \propto \rho^2$ } $T^2/R \sim$ const.

$T_{dead} \propto \rho e^{-(\rho\ \delta t)}$

$R_{dead} \propto \rho^2 e^{-(\rho\ \delta t)}$

Total throughput const.
NEC ~ $1/\rho^2$

More activity and efficiency does not always help !

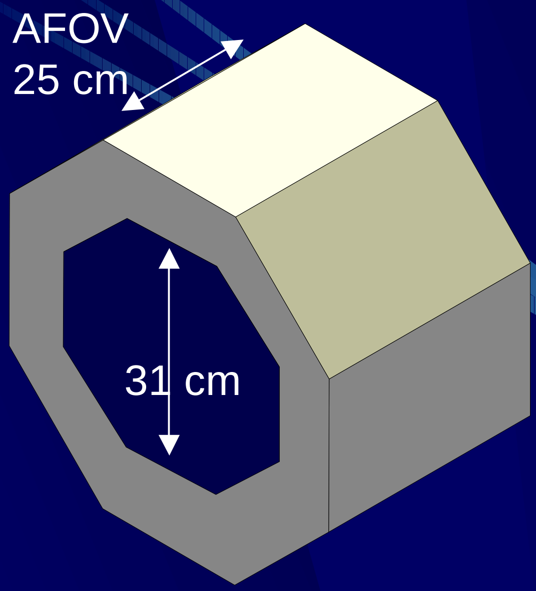
Courtesy of B. Moses, Mattinata 2002

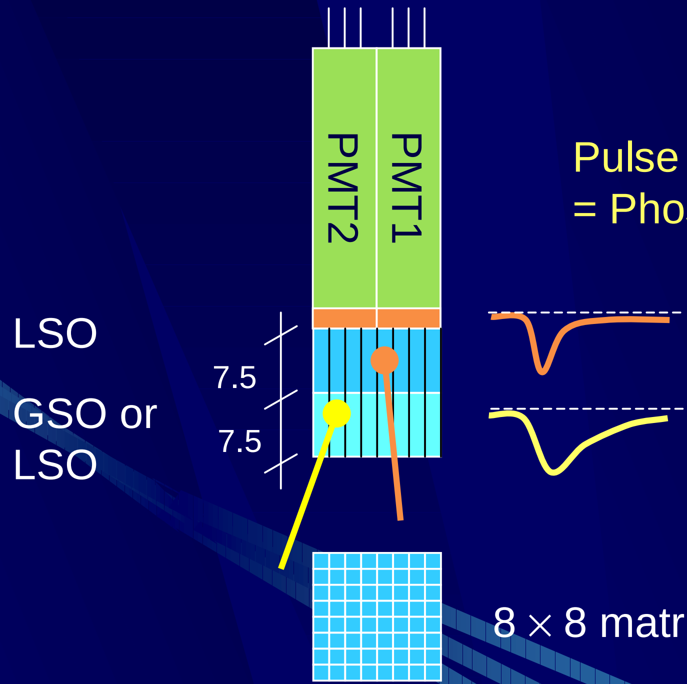
Concrete example: The High Resolution Research Tomograph (HRRT)

(CTI, MPI, Karolinska …)

K. Wienhard et al., **IEEE Trans. Nucl. Sci. 49 (2002) 104–10**

Currently the "reference" in brain PET





Pulse Shape Discrimination
= Phoswich approach

$\Delta\tau$ = 7 ns

8 $\times$ 8 matrix

- 8 panels with 9 $\times$ 13 blocks
- 2 $\times$ 64 crystals per block
- Crystal dimensions: 2.1 $\times$ 2.1 x 7.5 mm

DOI is known with a precision of 5 mm (FWHM), 10 mm without phoswich.

However 15 mm detector length correspond only to about 1 λ_a.
Efficiency ε_2 ~ 40%

HRRT performance

- spatial resolution (FWHM)
  - transaxial: 2.4 - 2.9 mm
  - axial: 3-4 mm

measured by moving a ^{18}F point source (1 mm Ø) over a cylinder of 20 cm diameter and 20 cm length

- Energy resolution: 17%
- Sensitivity: 4.5 cps/kBq
- NEC: 140 kcps

cylinder of 20 cm diameter and 20 cm length filled with ^{18}F dissolved in water to an activity of 0.35 μCi/ml.

Hybrid Photon Detectors (HPD)

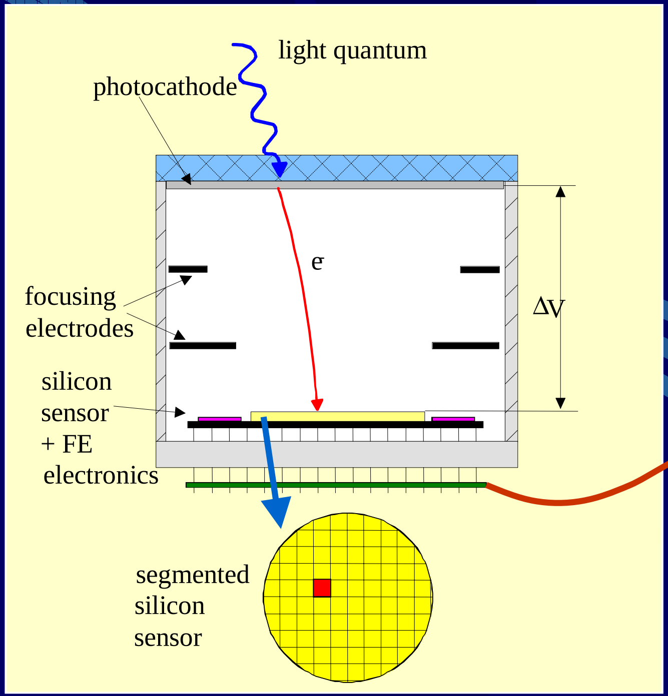
Background:

Applications in LHC experiments require photon detectors featuring

- High sensitivity in visible and UV range
- Ability to see single photons
- high speed (remember 40 MHz bunch crossing)
- High filling factor (>70%)
- Large area coverage (~m^2)

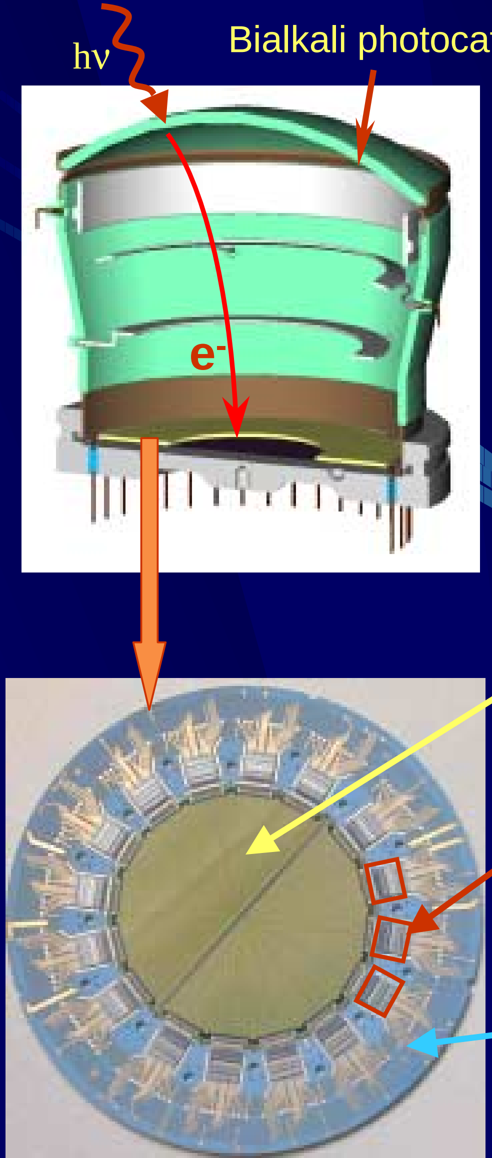
→ Development of large area Hybrid Photon Detectors

Combination of sensitivity of PMT with excellent spatial and energy resolution of silicon sensor



The 5-inch Pad HPD

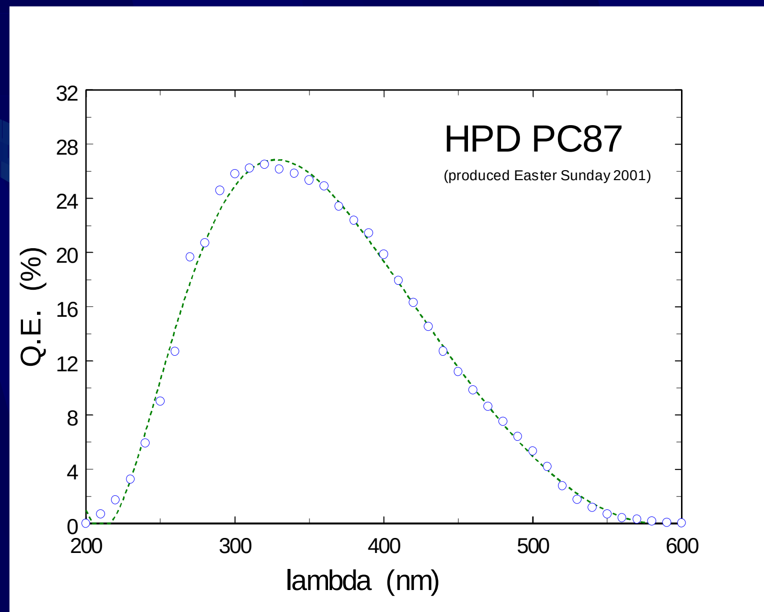
Bialkali photocathode



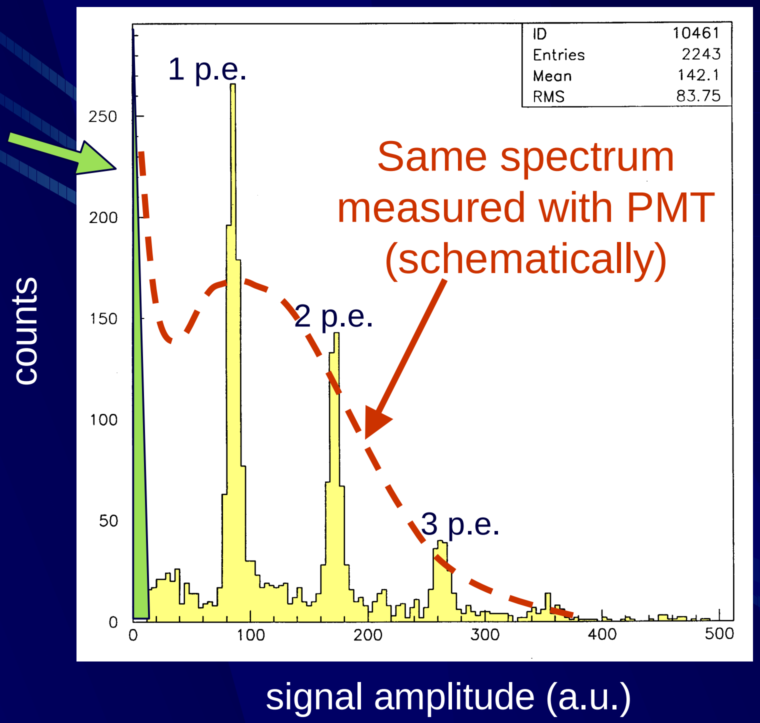
Si Sensor
2048 pads
(1 x 1 mm^2)

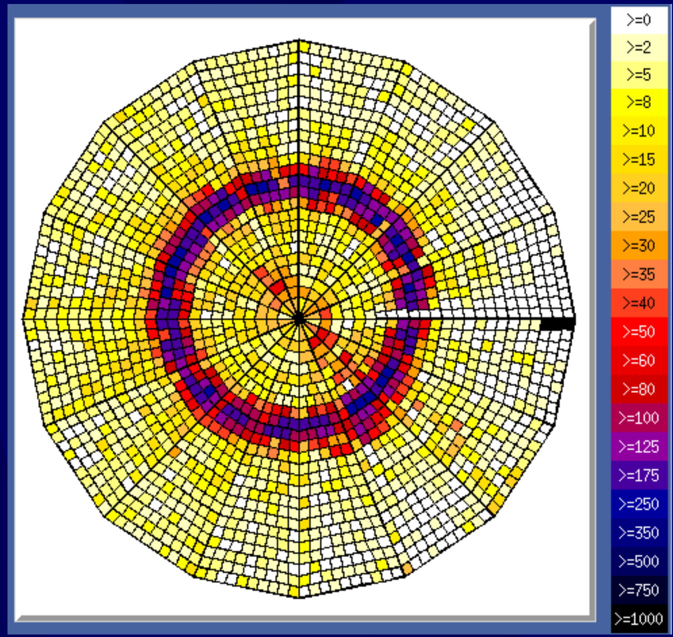
16 front-end chips

Ceramic PCB



Electronics noise well separated from signal



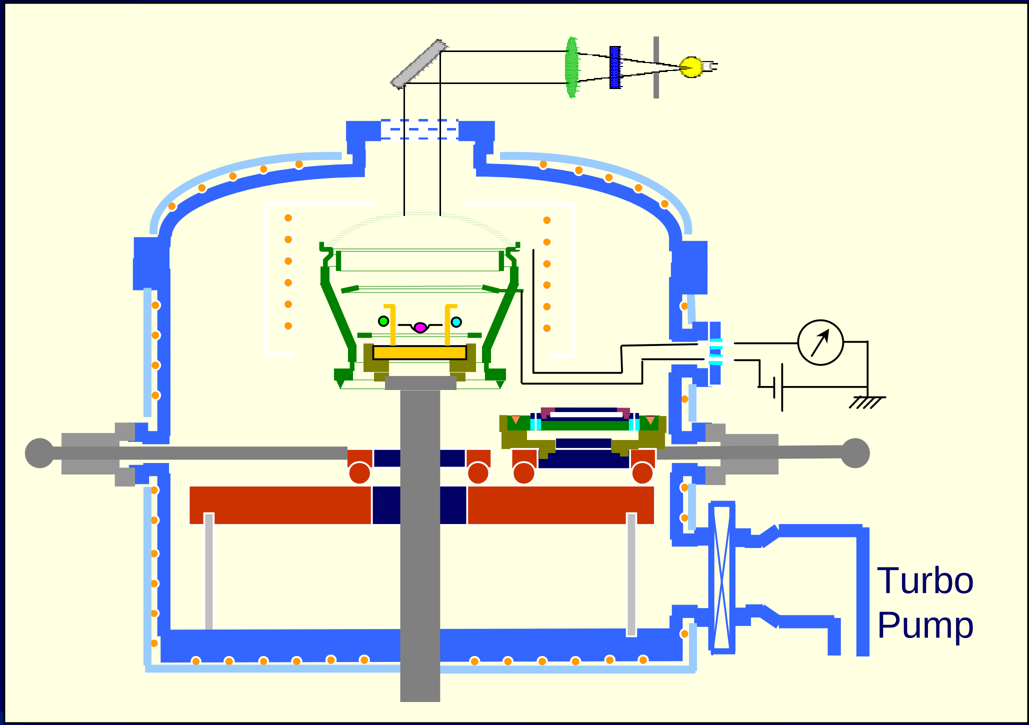


Signal definition and energy resolution.
S/N ~ 10.

Single photon imaging with 2048 Channels.

HPD fabrication

Facilities and infrastructure for the fabrication of large HPDs (up to 10”Ø) have been developed at CERN.

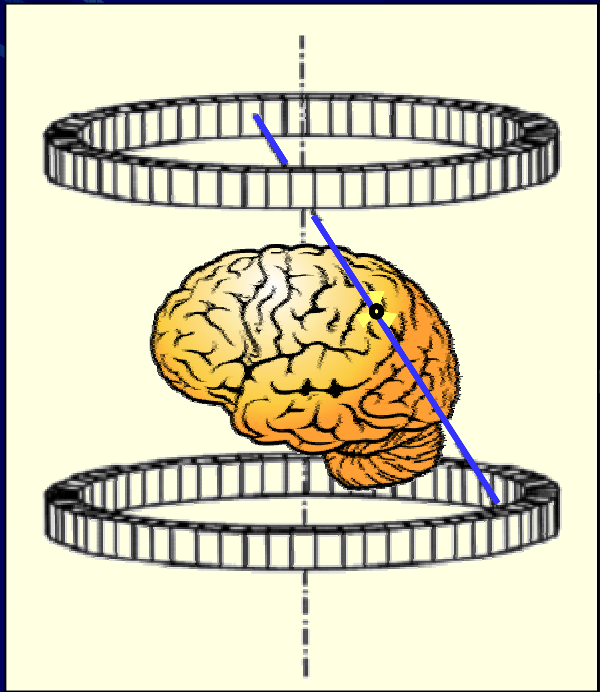


All ingredients for photodetector production are available:

- Design/simulation
- Photocathode processing (bialkali, Rb_2Te, CsI)
- Glass / ceramic tube manufacturing
- Indium sealing technique

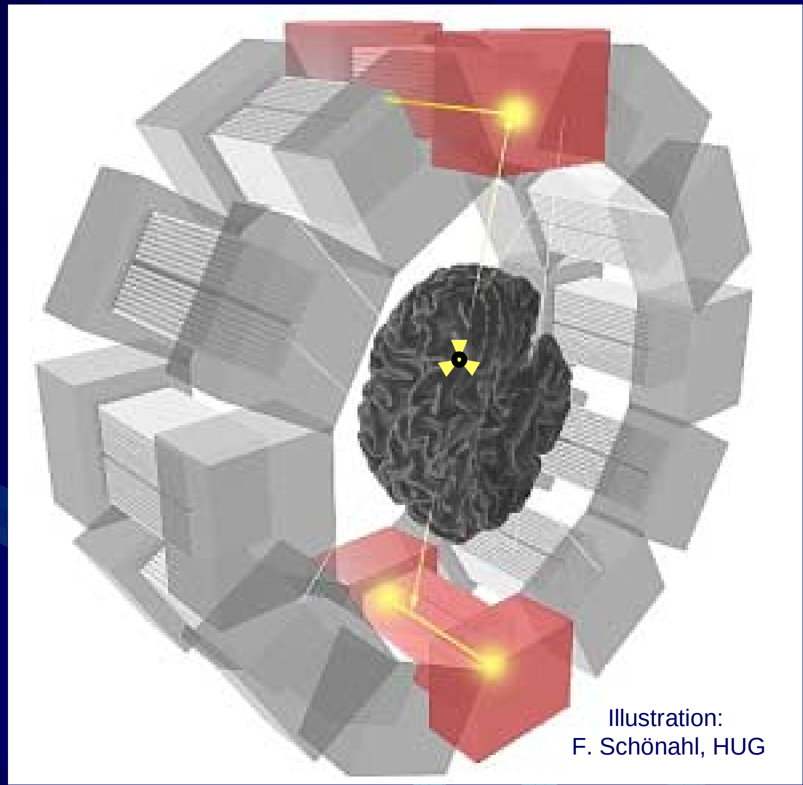
The 3D axial PET camera

Conventional concept



Rings of block detectors

New 3D axial concept



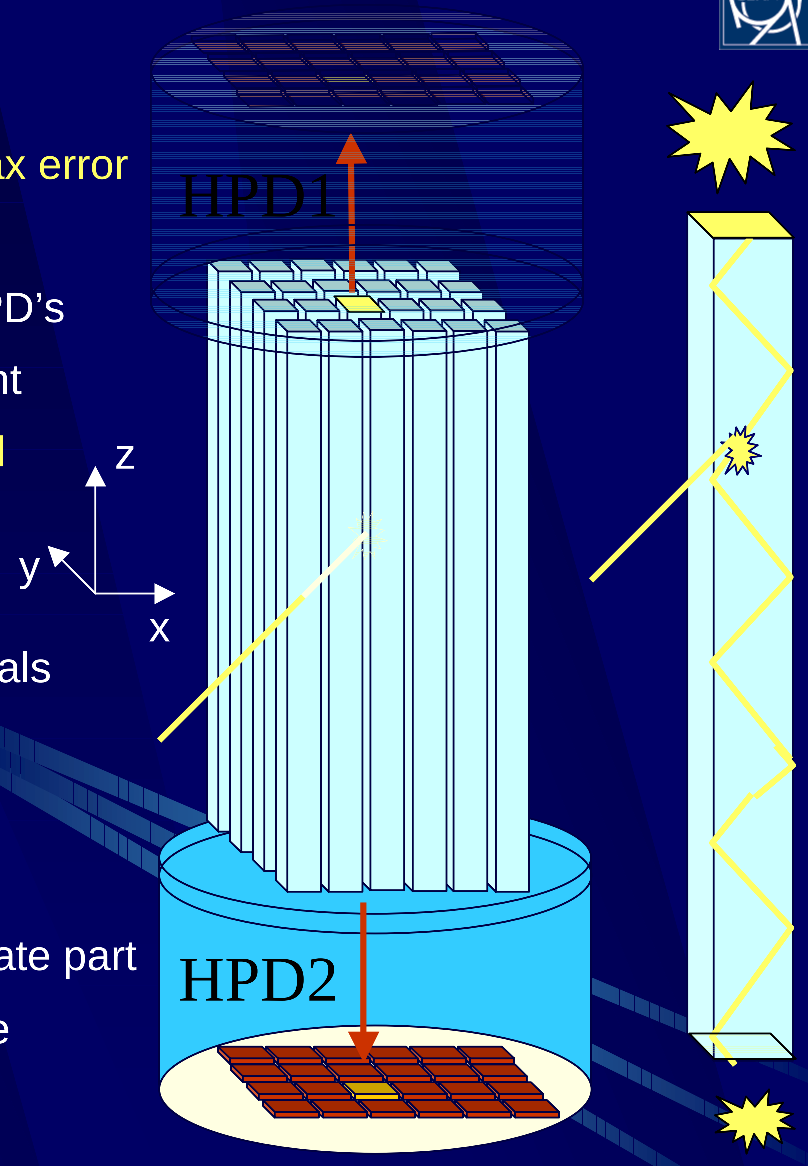
Axial arrangement of camera modules based on matrices of long crystals read out on both sides by HPDs

Main advantages of the concept

- Full 3D reconstruction of γ quanta without parallax error
  - x,y from silicon pixel address
  - z from amplitude signal ratio of the 2 HPD's

  ➨ Precise Depth of Interaction DOI measurement

  ➨ No limitation in detector thickness ➨ improved sensitivity.



- Measurement of light yield on both sides of crystals
- Negligible statistical fluctuations in HPD

  ➨ Very good γ energy resolution

- 3D reconstruction provides possibility to recuperate part of γ's which underwent Compton scattering in the scintillator crystals

  ➨ Compton enhanced sensitivity

Critical aspects of the concept

- z-resolution scales with crystal length

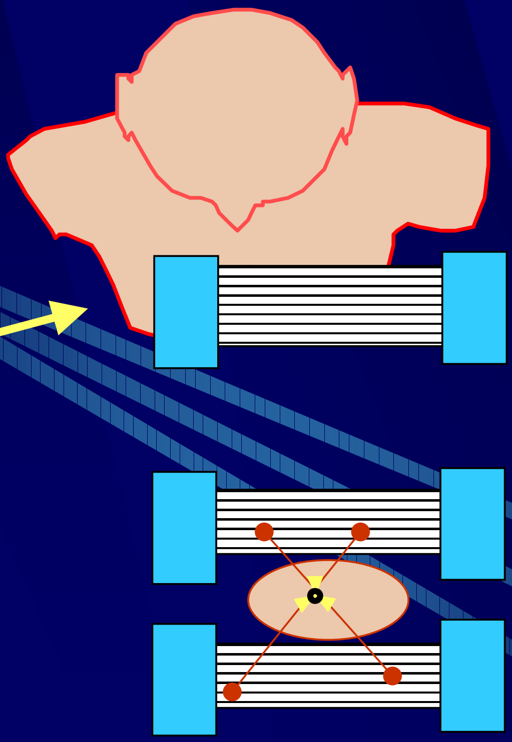
  $\sigma_z \sim L$

  ➔ Axial field of view limited to about 10 - 15 cm

- Little experience in fabrication of long crystals (cost)

The concept seems to be very promising for brain PET, where both high spatial resolution and high sensitivity are required.

PEM (PE mammography), in compressed mode, is another interesting option.



Scintillation crystals for the 3D axial concept

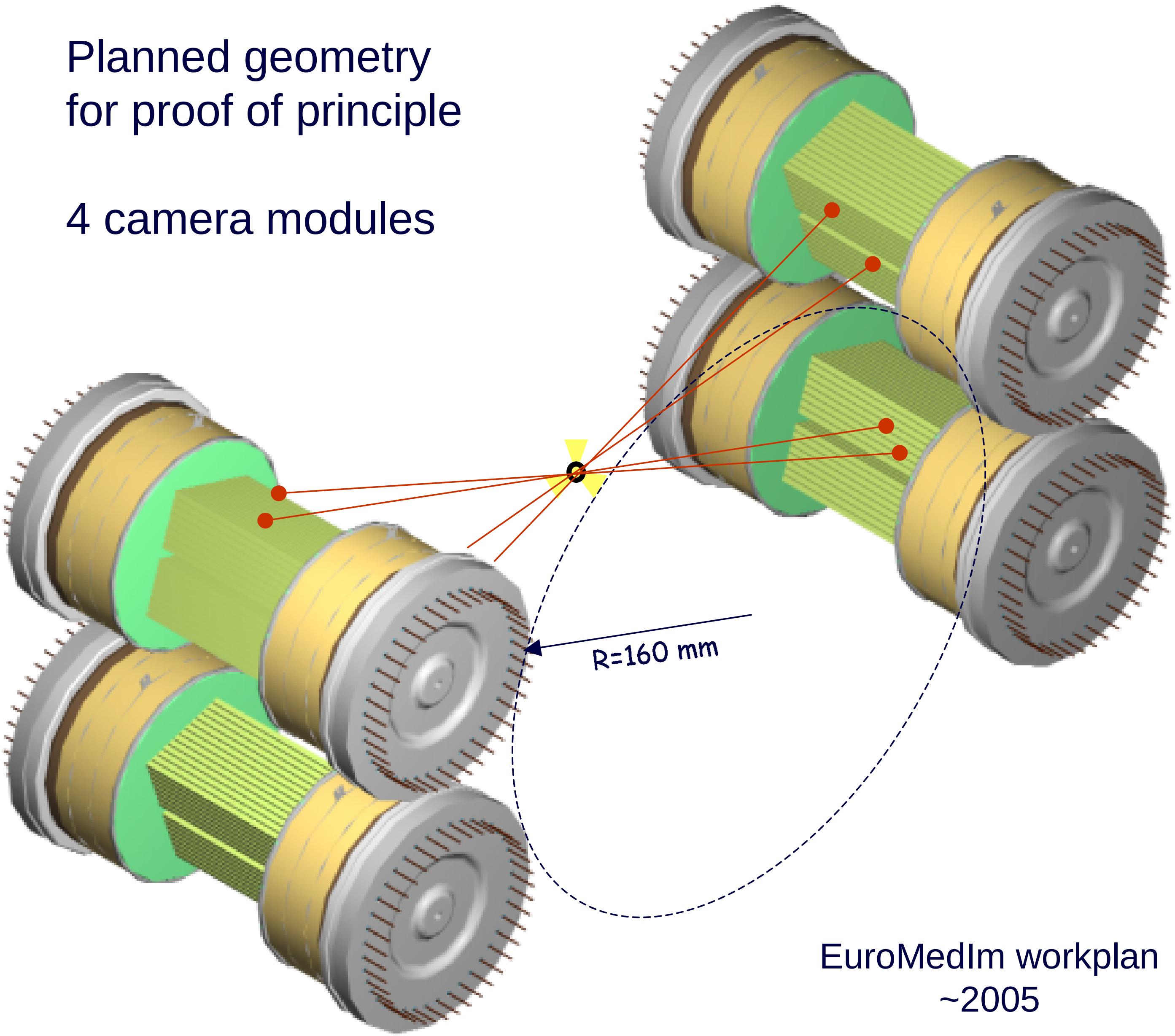
- Criteria to be taken into account: light yield, absorption length, photo fraction, self absorption, decay time, availability, machinability, price.

	YAP:Ce	LSO:Ce	LuAP:Ce	$LaBr_3$:Ce	BGO
Density ρ (g/cm^3)	5.55	7.4	8.34	5.3	7.13
Effective atomic charge Z	32	66	65	46.9	75
Scintillation light output (photons / MeV)	18000	23000	~10000	~61000	~9000
Wavelength of max. emission (nm)	370	420	370	356	480
Refractive index n at wavelength of maximum emission	1.94	1.82	1.95	~1.88	~2.15
Bulk light absorption length L_a (cm) at 370 nm	~14	~20			
Principal decay time (ns)	27	40	38	30±5	300
Mean γ attenuation length at 511 keV (mm)	22.4	11.5	10.5	~20	~11.6
Photo fraction at 511 keV (%)	4,5	32.5	30.5	15	41.5
Energy resolution at 663 keV	4.5	8		2.9	

- YAP is OK for proof of principle, however suffers from low Z (high absorption length, low photo fraction) All preliminary performance estimates are based on YAP (availability!)
- $LaBr_3$, LSO and LuAP are the really interesting candidates.

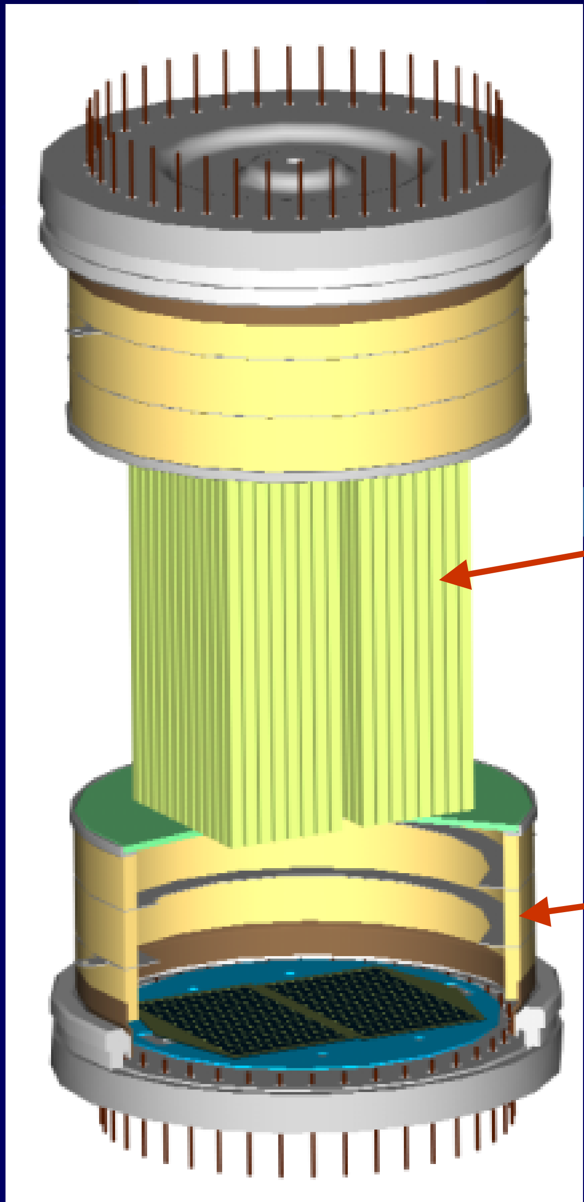
Planned geometry
for proof of principle

4 camera modules



EuroMedIm workplan
~2005

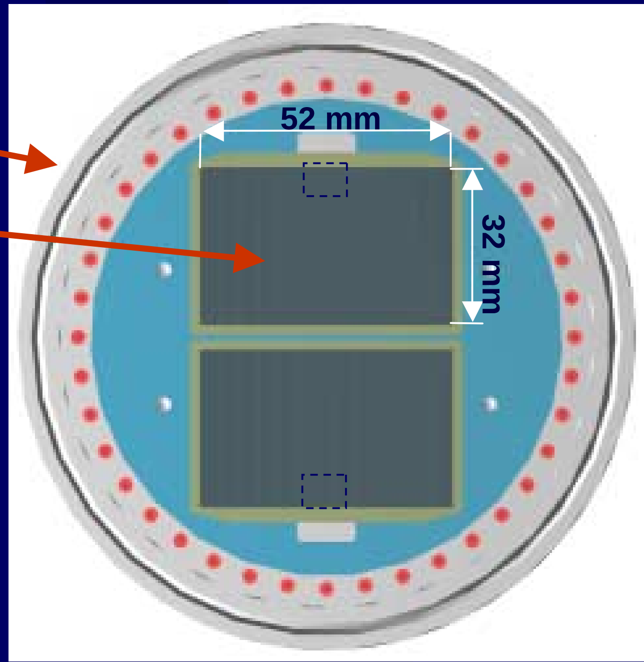
A camera module based on HPD PCR5



208 crystals (YAP)
3.2 × 3.2 × 100 mm^3
(ordered)

HPD PCR5

Baseplate (existing)
with
2 Silicon sensors
(existing)



Ceramic envelope
with sapphire
entrance window
(recently produced
at CERN)

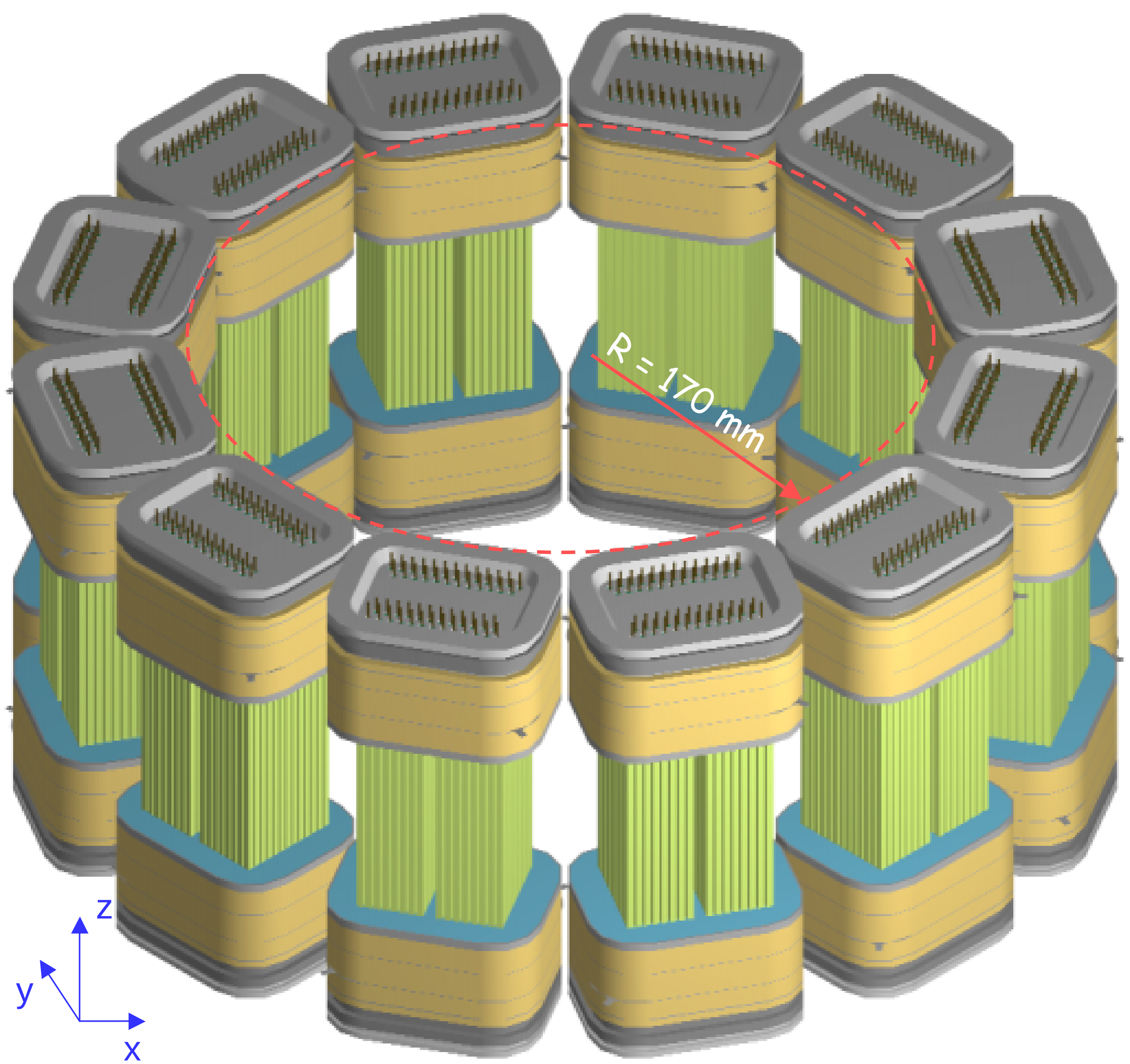
Full ring scanner

Possible configuration for a Brain PET

- 34 cm inner diameter
- 10 cm axial length
- 2496 crystals
- 24 HPDs
- total detection volume

  2556 cm^3
- Φ coverage 66%
- Ω coverage 18%

EuroMedIm
Workplan ~2007

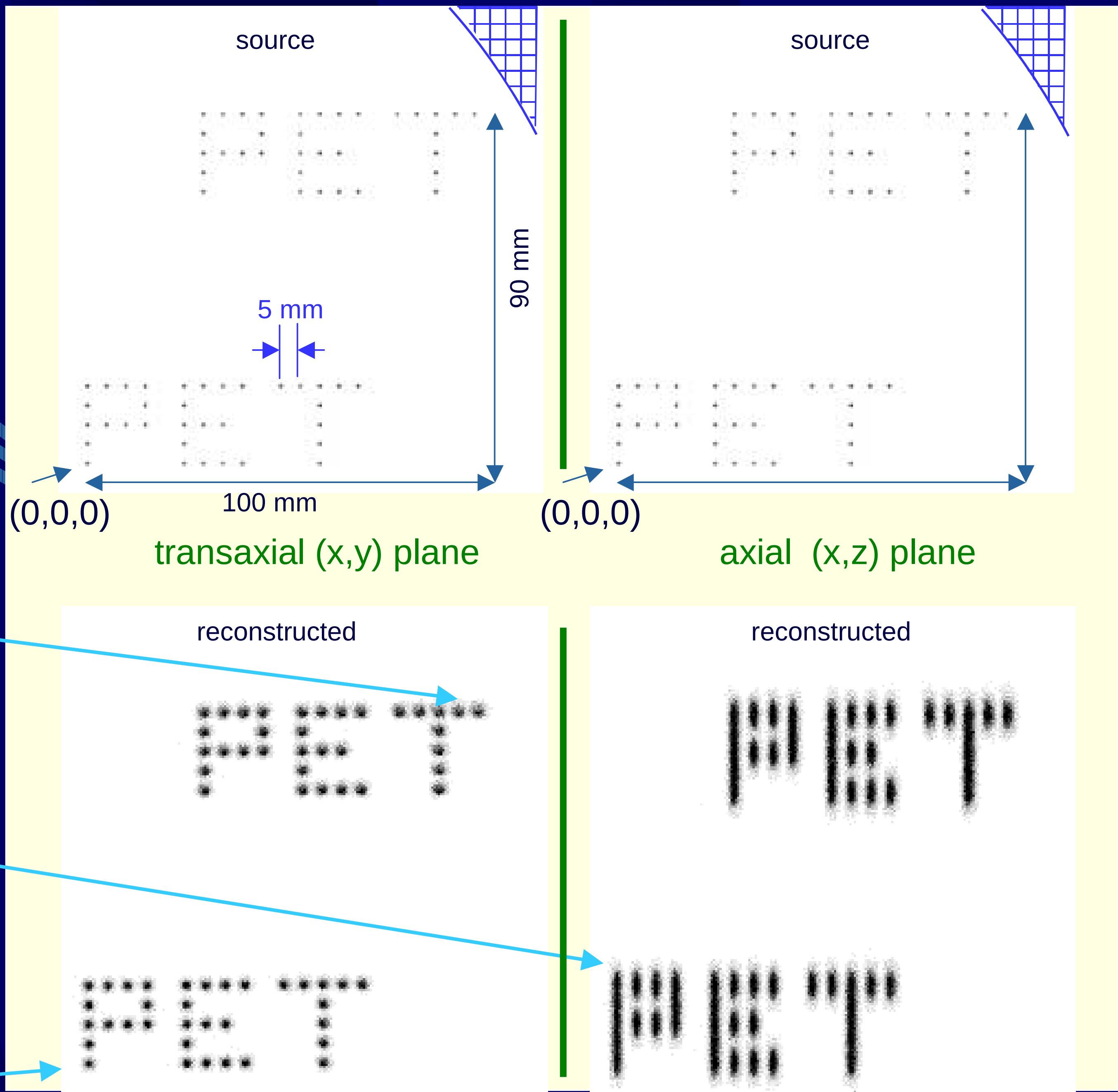


3D axial PET geometry

Crystal dimensions:
3.2 x 3.2 x 100 mm

Material: YAP:Ce

33 point sources,
no background



Resolution x,y
~2.2 mm

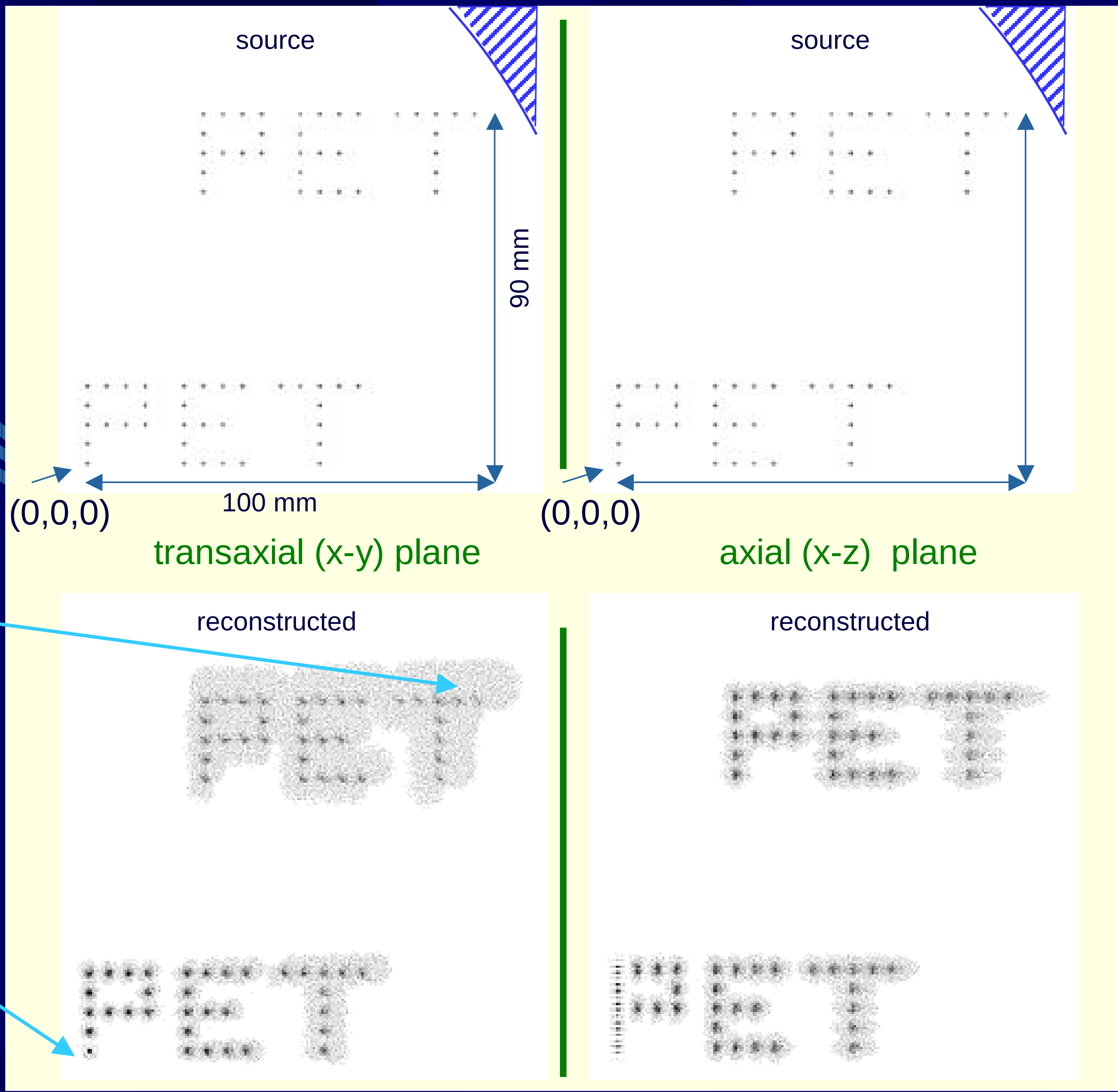
Resolution z
~4.5 mm

Resolution x,y
~1.5 mm

Standard PET geometry

Crystal dimensions:
3.2 x 3.2 x 30 mm

33 point sources,
no background



Resolution x,y
~6 mm FWHM

Resolution x,y
~1.5 mm FWHM

Performance estimates 3D Axial Brain PET (with YAP:Ce)

		(HRRT)
• Detected photoelectrons for a γ of 511 keV:	540 - 625 per HPD	(?)
• Energy resolution:	7 – 7.5 % (FWHM)	(17)
• Spatial resolution in transaxial plane:	1.5 - 2.2 mm (FWHM)	(2.4-2.9)
• Spatial resolution in axial:	4.5 mm (FWHM)	(3-4)
• Coincidence interval:	~ 5 ns	(≥2 ns?)
• Compton gain:	~ 2	(1)
• Sensitivity	3-4 cps/kBq	(4.5)
• NEC:	130 kcps	(140)

HPD based Brain PET should beat HRRT in spatial and energy resolution and should at least be comparable in other disciplines.

EuroMedIm

"Integrated Project". Proposal submitted (25 March 2003) in the 6th EU framework programme (FP6).

Proposal title

Targeting cancer by molecular imaging - R&D, construction and clinical validation of advanced multimodal imaging devices and radiopharmaceuticals for early detection, characterization and treatment follow-up of cancer diseases

The goal of this project is to develop a new generation of imaging detectors that would allow a non-invasive assessment of an accurate identity card of a cancer tumour without any need for ex-vivo analysis.

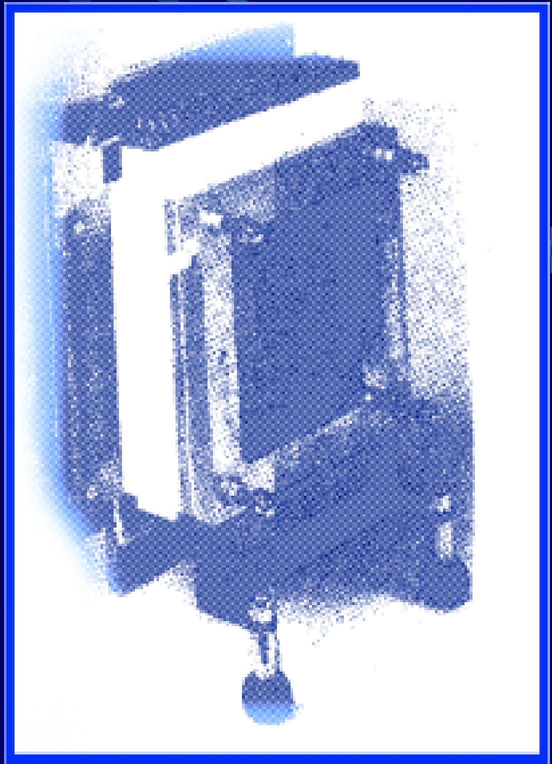
Multimodality, i.e. PET/CT, PET/MRI, CT/SPECT is in the main focus.

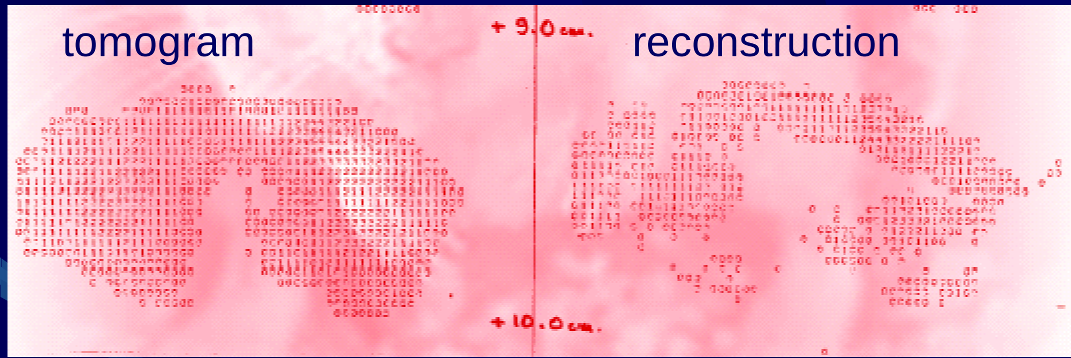
Aim for the "One-stop-shop" molecular profiling imaging device for the whole body.

EuroMedIm is a collaboration of ~60 research institutions (e.g. CERN), cancer centres, hospitals (e.g. HUG), small and large size industries (e.g. General Electric, Siemens).

CERN initiated and participates in the EuroMedIm project, because there is a large overlap between the requirements and the technologies developed for high energy physics and those needed in medical imaging.

There are examples of successful medical projects in the past, e.g.





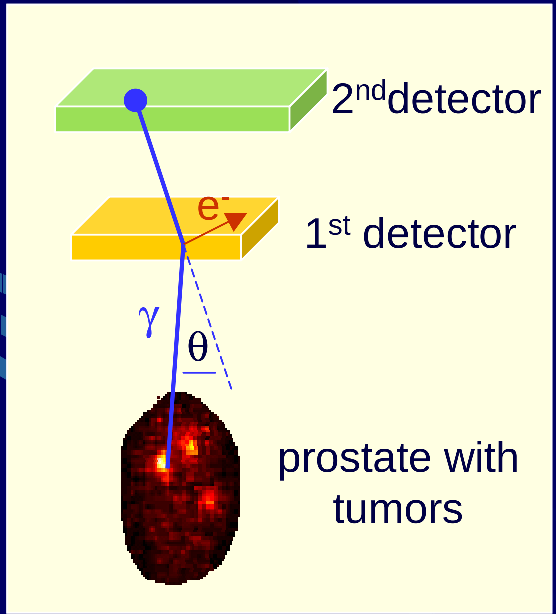
THE HIGH DENSITY AVALANCHE CHAMBER FOR POSITRON EMISSIONS TOMOGRAPHY,

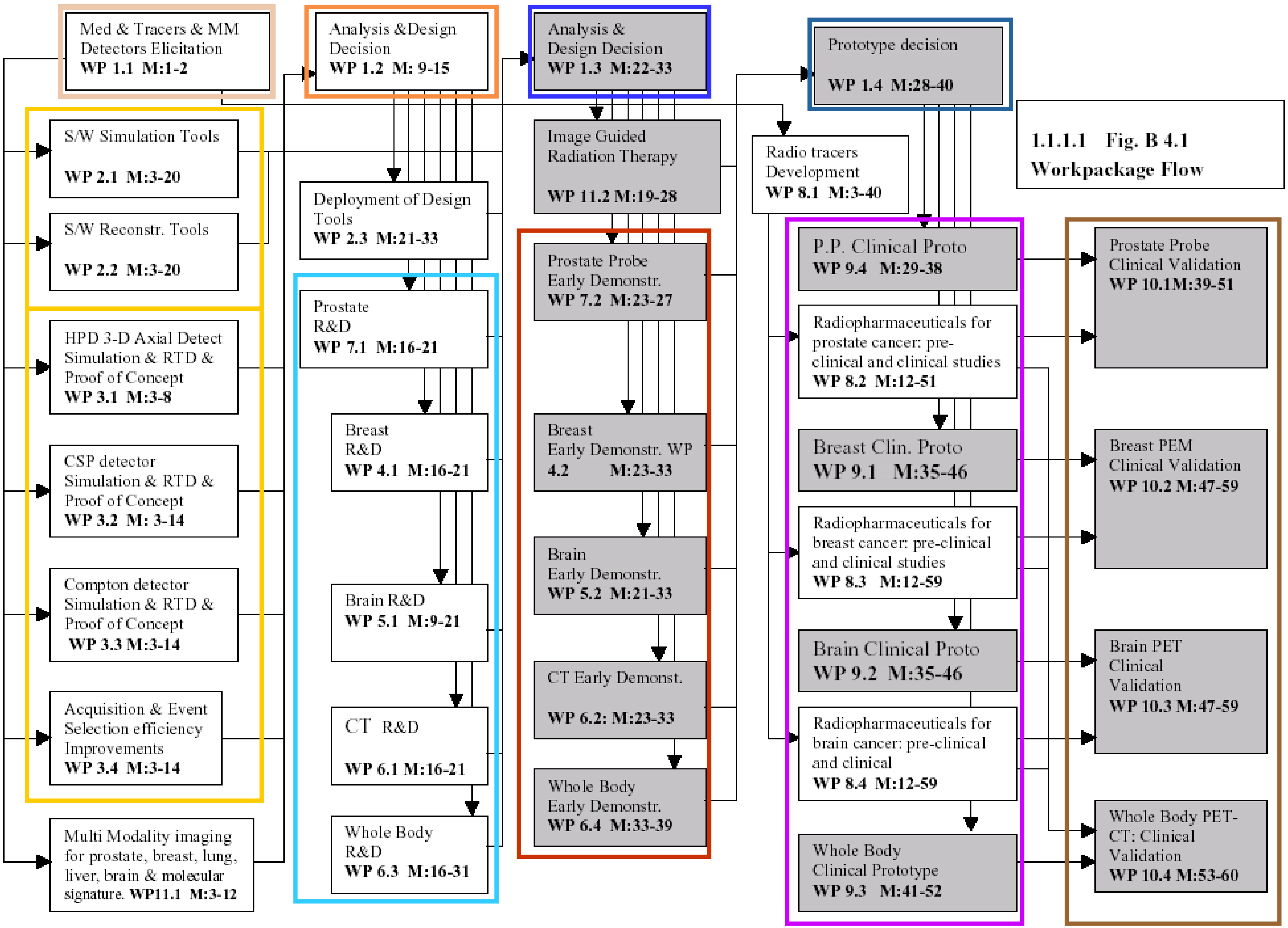
Jeavons (CERN), Townsend (HUG) et al., IEEE Trans.Nucl.Sci.30:640-645,1983

Spatial resolution 2.4 mm FWHM, Maximum data rate: 3000 c.p.s, Sensitivity: 0.67 c.p.s./ kBq

Apart from the HPD 3D axial PET (patent applied PCT/EP 02/07967),
EuroMedIm comprises the following technological developments …

- New optimized radio tracers
- Simulation and reconstruction tools
- Positron Emission Mammography, based on LuAP crystals and APD readout
- Novel CT detector, based on ASICs + amorphous Si layer (Patent applied PCT/EP03/00603 and PCT/IL/03/00125)
- Compton SPECT for prostate cancer “electronic collimation”
- Multimodality analysis and image fusion
- …




Med & Tracers & MM Detectors Elicitation WP 1.1 M:1-2
Analysis &Design Decision WP 1.2 M: 9-15
Analysis & Design Decision WP 1.3 M:22-33
Prototype decision WP 1.4 M:28-40
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HPD 3-D Axial Detect Simulation & RTD & Proof of Concept WP 3.1 M:3-8
CSP detector Simulation & RTD & Proof of Concept WP 3.2 M: 3-14
Compton detector Simulation & RTD & Proof of Concept WP 3.3 M:3-14
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Whole Body Early Demonstr. WP 6.4 M:33-39
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1.1.1.1 Fig. B 4.1
Workpackage Flow

The HPD PET collaboration

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