Demonstration of a novel PET concept

Chiara Casella, ETH Zurich DPNC - Université de Genève, March 14th 2012

Outline

AX-PET : AXial Positron Emission Tomography (PET)

•Brief introduction about PET (Positron Emission Tomography)

•Axial concept

What is it ? Why?

•AX-PET detector

choice of the detector elements AX-PET modules "demonstrator" for a PET scanner

•AX-PET detector performance

from characterization measurements with 22-Na sources

Simulations

Tomographic image reconstruction

description of the reconstruction methods measurements campaigns with phantoms and radiotracers reconstructed images

Perspectives

preliminary results with **Digital Si-PM** as alternative photodetectors

Conclusions

AX-PET in the context of HEP

- Long tradition of using technologies from High Energy Physics into other fields, and particularly medical applications.
- AX-PET : small size calorimeter, using scintillating crystals, WLS, photodetectors "borrowed" from HEP

Selection of most relevant AX-PET papers :

| Novel Geometrical Concept of a High Performance Brain PET Scanner Principle, Design and Performance Estimates J. Seguinot et al, Nuovo Cimento C Vol 29, No 4, pp 429-463 (2006) | axial concept, Hybrid Photo Diodes (HPD) readout |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| High precision axial coordinate readout for an axial 3-D PET detector module using a wave length shifter strip matrix A. Braem et al, NIM A 580 (2007), 1513-1521 | WLS strips |
| Wavelength shifter strips and G-APD arrays for the read-out of the z-coordinate in axial PET modules A. Braem et al, NIM A 586 (2008), 300-308 | G-APD as photodetectors |
| The AX-PETdemonstrator—Design, construction and characterization P. Beltrame et al, NIM A 654 (2011) 546-559 | Characterization & performance |
| The AX–PET Concept: New Developments And Tomographic Imaging P.Beltrame et al, 2011 IEEE NSS Conference Record MIC 22-5 | Tomographic images |

for more details : https://twiki.cern.ch/twiki/bin/view/AXIALPET/WebHome

Positron emission / annihilation



b"back - to - back"

 \blacktriangleright EY = 511 keV

Physics of the positron annihilation => fundamental limits to the spatial resolution of PET

Finite positron range (ρ)

annihilation position \neq emission point

 ρ depends on the energy of the positron (i.e. on the radioisotope)

Non-collinearity of the 2 photons

residual momentum of the e+e- at the annihilation the 2 photons are emitted with a small deviation from 180° ($\Delta\theta \sim 0.5^{\circ}$) blurring of the spatial resolution R_FWHM ~ 0.0022 x D [mm]

Positron Emission Tomography : General principles

PET detector principle :

coincidence of 2 photons of defined energy (511 keV) and emitted on the same line ("back to back")



(1) Inject the radiotracer into the body

- (2) Wait for uptaking period
- (3) Start the acquisition (i.e. **detection of coinc. events**)
- (4) Feed the data into the reconstruction algorithms
- (5) image of the activity concentration

full body / brain

- clinical applications
 oncology (tumor diagnosis)
 - neurology (e.g. brain disease diagnosis)
 - map normal human brain / heart functions

small animal

pre-clinical studies

scanners

scanners

- cancer research
- new tracers development
- pharmacokinetics

PET : "in-vivo" functional imaging technique

get a (quantitative) image of the radio-tracer concentration



Requirements for an ideal PET

number of counts does matter !!!



- how to improve counting statistics ?
 - ▶ increase radio-tracer concentration
 - extend the scan duration time

OPTIMIZED DETECTOR SENSITIVITY

(geometry / materials)

HIGH SPATIAL RESOLUTION (=> be able to resolve small structures)

- GOOD TIMING RESOLUTION (small coincidence window => reduce random coincidences)
- GOOD ENERGY RESOLUTION (=> reject scattering events in the body)

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GOOD ENERGY RESOLUTION (=> reject scattering events in the body)



always a compromise between > good spatial resolution (small L, small δp)
 > good detection efficiency (long L)

solution : add DOI (Depth Of Interaction) information

several attempts / different strategies

Conventional PET schemes

DOI attempts :





(a) **multiple** crystals/ photodetector **layers**

(b) **dual-ended photodetectors** DOI from the ratio of the 2 PD responses



 (c) Phoswich design different types of crystals with diff decay times
 => DOI from pulse shape discrimination (d) **monolithic.** Iterative stat. models with DOI from light output intensity and/or light spread profiles





Peng, Levin - Current Pharmaceutica Biotechnology, 2010, Vol 11, No. 6

(e) dual layer offsetposition.DOI from different light outputprofiles

only partial DOI information !

need a precise 3D identification of the photon interaction point

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The AXIAL concept

AX-PET approach to the DOI problem : change the geometry !





- Iong and axially oriented crystals
- DOI information = position of the hit crystal

The detector concept



- Transaxial coordinate: from position of the hit crystal

- Transaxial resolution = $d/\sqrt{12}$ FWHM

To increase spatial resolution => Reduce crystals size (d)
To increase sensitivity => Add additional layers

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The detector concept



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> 'escaping cone' (outside total

internal reflection)

Ζ

crystal

(2) AXIAL COORDINATE (z)

scintillation process

photodetector

- Axial resolution < w

The detector concept

WLS (Wave Length Shifter) array



- Transaxial coordinate: from position of the hit crystal - Transaxial resolution = $d/\sqrt{12}$ FWHM

- To increase spatial resolution => Reduce crystals size (d) - To **increase sensitivity** => Add additional layers

3D localization of the photon interaction point without compromising between spatial resolution and sensitivity



reflective Al

coating

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AX-PET Collaboration









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AX-PET GOAL : PET demonstrator

Goal of the AX-PET collaboration:

Build and fully characterize a "demonstrator" for a PET scanner based on the axial concept. Assess its performances.

Demonstrator => Two identical AX-PET modules, used in coincidence

Characterization / Performance =>

- test each individual module in a dedicated setup
- characterization in the coincidence setup
- reconstruction of the images of extended objects
- simulations

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Detector choice: Scintillator

detect photons, $E_{Y} = 511$ keV

- => inorganic scintillator
 - high Ζ, high ρ
- bare scintillating crystals with escaping light =>
- non hygroscopic
- nude crystals (i.e. unwrapped, uncoated)
- perfectly polished surfaces ; sharp edges

LYSO crystals (Lu_{1.8}Y_{0.2}SiO₅: Ce) Prelude 420 from Saint Gobain :





I 76-Lu is a naturally radioactive β emitter (A ~ 39 Bq/g; β-decay followed by a γ-cascade) useful for the calibration

- lyso bars : 3 x 3 x 100 mm³ each
- Al coated on the non-readout face (R \sim 80-85%)
- measured : $\lambda_{opt} = (412 \pm 31) \text{ mm}$; ($\Delta E/E$)_intr = (8.3 ± 0.5) % FWHM, @511 keV

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Detector choice:WLS strips

• requirement : high absorption of the crystal scintillation photons (blue)

• EJ-280-I0x from Eljen Technology

- blue to green WLS
- highly doped (x10 higher dye concentration than standard) to maximize the absorption (absorption length _ blue light ~ 0.4 mm)
- each WLS strip : **3 x 0.9 x 40 mm³**
- decay time = 8.5 ns

• measurements : $\lambda_{opt} = (188 \pm 36)$ mm





Detector choice: Photodetectors

newest frontier in photo-detection: SiPM (Si photomultipliers)

SiPM (Si photomultipliers) also called **G-APD** (Geiger-mode APD)

also called **MPPC** (Multi Pixel Photon Counter) - from Hamamatsu



- array of commonly biased APD used in Geiger mode
- output : analogue sum of all the firing APD cells
- excellent photon counting capabilities $\sqrt{}$
- high gain (10⁵ to 10⁶) at low bias V (~ 70 V) $\sqrt{}$
- advantages of a Si sensor:
 - high QE
 - \blacktriangleright compactness \checkmark
 - insensitive to magnetic field (MRI comp.) $\sqrt{}$
- temperature dependent $\sqrt{}$
- dark rate (~ I MHz @ thr = 0.5 pe) $\sqrt{}$

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MPPC \$10362-33-050C :

- 3x3 mm² active area
- 50 µm x 50 µm pixel
- 3600 pixels

MPPC 3.22×1.19 Octagon-SMD :

- 1.2 x 3.2 mm² active area
- 70 µm x 70 µm pixel
- 782 pixels
- custom made units

| | crystal MPPC | WLS MPPC |
|----------------------|--------------------------------|---------------------------------|
| type | S10362-33-050c | custom tailored |
| charge gain G | $6 \cdot 10^{5}$ | $1 \cdot 10^{6}$ |
| dG/dV | $55 \cdot 10^4 \text{ V}^{-1}$ | $110 \cdot 10^4 \text{ V}^{-1}$ |
| noise rate at 0.5 pe | 4.7 MHz | 3.2 MHz |
| noise rate at 1.5 pe | 0.9 MHz | 0.5 MHz |

Table 1: Main characteristics of the MPPCs. Gain and noise rates refer to temperature of 25°C.

AX-PET operational parameters



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The AX-PET module



- 8 crystals / layer
- 26 WLS / layer
- 48 crystals + 156 WLS = **204 channels**
- staggering in the crystals layout to optimize photon interaction probability
- optical separation between layers
- each crystal and WLS strip individually coupled to its photodetector
- crystals / WLS strips readout on alternate sides (to optimize packing density)

3.5

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The AXPET module



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Readout & DAQ

Individual analogue readout of MPPC output Custom designed DAQ system

- fully analogue readout chain
- not optimized at all for this specific application
- Amplifiers: OPA486 (Lyso) / OPA487 (WLS)
- Fast energy sum for all the crystals in the module
- VATA GP5 chip
 - 128 ch charge sensitive integrating
 - fast (~ 50ns shaper + discriminator) / slow (~ 250ns shaper) branches
 - **sparse readout** mode: only the channels above thr are multiplexed into the output
- analogue info processed by custom made VME ADC





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Fast energy sum & Trigger



Mod 1, energy sum (scope measurement), ²²Na source

TRIGGER



TRIGGER = 2 modules

- each one discriminated @ 511 keV energy sum
- used in coincidence
- => Selection of the good events

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Compton scattering

Compton scattering in the detector

- fast energy sum & trigger
- high granularity in the module
- good energy resolution

Possibility to tag Compton scattered events in the detector

"Inter-Crystal Scattering" events (ICS)



if the event is :

correctly identifiable (e.g. Compt. kinematics)

=> the event can be included in the reconstruction

 $E_1 + E_2 = 511 \text{ keV}$

 $E_1 + E_2 = 511 \text{ keV}$

=> improved sensitivity

win - win situation !

• ambiguous (1-2 OR 2-1 ?)

=> the event is rejected

=> improved resolution

Compton scattering in the body

Events killed by the trigger !



AX-PET inspired other developments

COMPET:



- no axial geometry
- 3D reco of photon interaction point with LYSO + WLS + G-APD

E. Bolle et al, NIM A 648(2011) S93-S95

Tampere University (Finland) :

build a small specific scanner based on AX-PET (toward possible commercialization...)

Low cost planar detector for PET

Triumph, Canada - F. Retiere et al.

F. Retiere, NIM A (2011) doi:10.1016/j.nima.2011.12.084



MPET



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Characterization measurements

with point-like ²²Na source (diam = 0.25 mm, A~900 kBq) , @ CERN



- two different taggers
- different distances tagger / source / module
- => both uniform illumination of the module and precisely collimated beam spot

AX-PET performance:

NIM A 654 (2011) 546-559

- I. Energy measurement / energy calibration => LYSO response
- 2. Position measurement / spatial resolution => WLS response

LYSO No. 21 - 22Na coinc. trigger

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LYSO energy response

Energy resolution 450 all events 400 H N_lyso = 1 from gaussian fit of the photopeak photopeak fit: gaussian 350 ▶ AFTER ENERGY CALIBRATION 300 Lu X-ray 250 Compton **Energy resolution** 200 [%] 14 [%] 13.5 13 13 13 13 13 14 13 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14 <li Module 1 150 Module 2 100 50 0^t 0 200 300 400 500 600 700 100 **ADC** counts < 511 keV 11.5 55 keV typical energy spectrum of one LYSO inside the module : 11 511 keV photopeak (511 keV) 10.5 Compton continuum (0 - 340 keV) 10[[] 20 40 60 80 100 ▶ Lu X-ray peak (~ 55 keV) 511 LYSO_ID keV 511 keV **II.8%** @511 keV < R FWHM > ~ Light yield at 511 keV ~ 1000 pe (averaged on 96 LYSO crystals) (from independent calibration measurements)

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LYSO energy calibration

Photopeak + Intrinsic Lu radioactivity: very good tool for the energy calibration



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WLS response

typical integrated raw spectra of few WLS strips

- beam spot collimated at the center of the module (WLS 13)
- 511 keV energy deposition in the LYSO



derived from <u>center of gravity method</u> from all the WLS participating to the cluster



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Two modules coincidences



AX-PET very first coincidence event !

Two modules coincidences



SIDE View - d(Mod1,Mod2) = 150 mm

Two modules coincidences

TOP View - d(Mod1,Mod2) = 150 mm[uu] / [uu]z N_coinc_evts=100 N_coinc_evts=100 50 50 0 0 -50 -50 -100 -100 -100 -50 0 50 100 -100 -50 0 50 100 X[mm] X[mm]

Axial resolution



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• AXPET performance • O

O simulations (

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Parallax free demonstration



parallax error is more and more important outside the center of the FOV



intersection of LORs with the plane containing the source



Intrinsic resolution is not degraded by parallax effects, even in very oblique configuration !

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Simulations

AX-PET is a fully simulated system

Dedicated Monte Carlo simulations for AX-PET .

- Why? (1) get a better understanding of the detector
 - (2) train Compton reconstruction algorithms
 - (3) support image reconstruction
 - (4) simulate an hypothetical full ring scanner and estimate its potential performance



GATE simulation package (Geant4 application for tomographic emission)

Non conventional nature of AX-PET

- => several challenges for simulations (standard templates could not be applied)
 - geometry (axial; staggering; layered structure)
 - WLS modeling
 - dedicated sorter for the coincidences (module sum; trigger logic... up to DAQ rate modeling)
○ simulations ○ image re

All Lyso

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No. Lyso

Simulations: some results

Excellent agreement data / simulations :

One AXPET Module illuminated by a collimated 511 keV gamma beam : Data and Simulations





Two AXPET Modules in coincidences



- identify ICS events before image reconstruction.
- several identification algorithms tested

| Max. E | Compton K. | Klein-Nishina | Neural Networks |
|--------|------------|---------------|-----------------|
| 61% | 65%-66% | 61%-63% | 75% |

• identification rate for ICS $\sim 60\%$

simulations paper is in preparation !

Towards a tomographic reconstruction...

How to mimic a full scanner with 2 modules only available?

Central FOV :

rotating the phantom...



θ = 0°, 20°, 40°... 180° **(9 steps)**



θ = 0°, 20°, 40°... 360° (**18 steps**)



I tomographic acquisition = 27 steps acquisition



mimics a 18-modules ring, with coincidences between face-to-face ± one adjacent modules

Setup for tomographic reconstruction



The two modules are mounted on top of a portable platform, which houses also the electronics, power supply, etc...

• One rotating motor for the source / phantom

• One module fixed (Mod I); the other rotating (Mod2)





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Measurements with phantoms

Three different measurement campaigns :

@ ETH Zurich (CH), Radio-Pharmaceutical Institute - Apr 2010

@ AAA (Advanced Acceleration Applications) St. Genis-Pouilly (FR) - July 2010

@ AAA (Advanced Acceleration Applications) St. Genis-Pouilly (FR) - July 2011

in-situ cyclotron production of the radiotracer.

- Phantoms filled with **F-18** based **tracers** (F-18 in water solution)
- t_{1/2} ~ 110 mins
- Concentration diluted in water; A₀: few MBq up to ~ 100 MBq

Measurements with phantoms

Three different measurement campaigns :

@ ETH Zurich (CH), Radio-Pharmaceutical Institute - Apr 2010

very first measurements with high activity and extended objects
limited to the **central FOV** (i.e. fixed modules, rotating source)

@ AAA (Advanced Acceleration Applications) St. Genis-Pouilly (FR) - July 2010

- extended FOV coverage (one module rotating, rotating source)
- larger phantoms / placed off-centered phantoms

@ AAA (Advanced Acceleration Applications) St. Genis-Pouilly (FR) - July 2011

- extended FOV as before
- **improved DAQ** performance
- improved acquisition methods

in-situ cyclotron production of the radiotracer.

- Phantoms filled with F-18 based tracers (F-18 in water solution)
- t_{1/2} ~ 110 mins
- Concentration diluted in water; Ao: few MBq up to ~ 100 MBq

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Phantoms for reconstruction



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Image reconstruction

Goal :

recover the activity distribution, starting from the acquired data

Data :

LOR of the various coincidence events i.e. **projections** (typically organized in "sinograms")



Two different approaches :

ANALYTICAL METHOD

- Filtered Back Projection (FBP) :
 - I) Fourier analysis of the projection data
 - 2) Different weight to different frequencies ("filtering")
 - 3) "Back-Project"
- simple and fast \bigcirc

• not extremely accurate 🔅

• assumption : measured data are perfectly consistent with the source object (never true: e.g. noise, gaps between detector...)



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derive from such an object



obtain the projection that would derive from such an object



obtain the projection that would derive from such an object



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Simple reconstructed images : capillaries

70

30

Distance [mm]





40 5 Distance (mm) O simulations O image reconstructions

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NEMA phantom

extended FOV 2nd module rotation

Three regions in the same phantom to address three different aspects

Hot & Cold rods for **contrast**

Homogeneous cylinder for assessing the ability to reconstruct homogeneous distributions



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Resolution phantom : Mini Deluxe





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Results presented in Valencia, IEEE 2011

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What's next (1/3) ?

- improve the reconstruction algorithms
- include ICS (Inter Crystal Scattering) events in the reconstruction



- ICS included:
 - only "triple" coinc. (I+2)
 - simplest weighting (50%; 50%)
- Simulated One-Pass List-mode reconstruction (SOPL)
- No image deterioration when ICS events are included!



SOPL + ICS





What's next (2/3) ?

• full ring simulations:

- performance of (hypothetical) full ring (e.g. resolution, sensitivity, NEC...)
- two different approaches



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What's next (3/3) ?

• images of (probably dead) small animal

- new measurement campaign
- @ETH Zurich, Radiopharmaceutical Institute
- Spring 2012 ?
- F-18 (bone scan) or FDG ?





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OD-SiPM

What's next (3/3) ?

• images of (probably dead) small animal

- new measurement campaign
- @ETH Zurich, Radiopharmaceutical Institute
- Spring 2012 ?
- F-18 (bone scan) or FDG ?





test digital Silicon Photomultipliers (from Philips) as alternative photodetectors

- extremely good timing performance
- GOAL : demonstrate the possibility a TOF-PET with the axial concept





OD-SiPM

D-SiPM:

Single Photon Avalanche

O conclusion

Digital Silicon Photomultiplier (D-SiPM)

PHILIPS

Digital SiPM – New Type of Silicon Photomultiplier





Digital Silicon Photomultiplier (D-SiPM)

Advantages of D-SiPM for AX-PET:

- Intrinsically very fast photodetector (~ 50ps).
 =>Great potential for TOF-PET.
- Small size. High level of integration.
- Compactness.
- Interesting concept of simplifying the readout chain. Bias supply included.
- Early digitization of the cell output; integrated electronics on chip => low noise.
- Digital => Temperature and gain stability is less critical than in analogue SiPM.
- Possibility to disable cells with high Dark Count.



Technology Evaluation Kit (TEK):



received at CERN on Jan 12th, 2012

• MRI compatible.

O conclusion

perspectives
 D-SiPM

D-SiPM: first preliminary results



- 2 LYSO scintillator crystals
 - non AX-PET standard
 - (2x2x12) mm³ and (2x2x15) mm³
 - wrapped with teflon
 - coupling done with optical grease
- LYSO crystal placed in the center of the pixel (no precise mechanical alignment)



(cutting on events at the photopeak)

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 D-SiPM

D-SiPM: first preliminary results

Minimal AX-PET like set-up





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D-SiPM: first preliminary results



• 2 tiles operated in coincidence

Correlation LYSO / WLS response

Still to do :

- add more WLS strips
- full WLS cluster
- extract axial coordinate



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D-SiPM: Outlook



two needed arrangements

Questions to be answered :

- light yield and $\Delta E/E$ from LYSO crystals ?
- axial coordinate reconstruction: does it work ?

coming soon...

- axial resolution through WLS readout ?
- time resolution (long crystals) ?



AX-PET performance demonstration

Conclusions

Axial concept for a PET scanner :

i.e. long and axially oriented scintillation crystals
 Intrinsically parallax free system (DOI information directly from the axial geometry)
 Spatial resolution and sensitivity could both be optimized

AX-PET implementation :

3D spatial information of the photon interaction point with : matrix of LYSO crystals and WLS strips individual readout of each channel (Si-PM)

Two modules built (i.e. **AX-PET demonstrator**) Energy resolution ~ 12% FWHM,@ 511 keV Spatial resolution ~ 1.35 mm FWHM

(competitive with state of the art PET)

calorimeter with tracking capabilities (granularity)

> novelty as a PET detector :

- geometry
- WLS implementation
- module sum / trigger
- Compton scattering reconstruction

Fully simulated device

Simulations - fully validated on the demonstrator - will assess the final performance of an hypothetical full ring scanner. **Flexible design**: scalable in size / dimensions / nr. layers.... => flexibility in the final target of AX-PET (small animal PET / brain PET)

AX-PET demonstrator : Extensively tested with sources and successfully used with phantoms !

Currently under test :

Digital SiPM as alternative for photodetector for AX-PET (TOF capabilities)

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photons, 511 keV

- inorganic scintillator

(high Z, high ρ , high light yield)

- unwrapped scintillator bars
- -WLS strips (for axial coord,)
- Si-PM

scintillator bars and WLS...

pions, 170 MeV (µ,e)

- organic scintillator (fast)
- WLS fibers embedded into scintillator bars (light collection and transport up to photodetectors)

FAST

- MA-PMT
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Conclusions









AX-PET collaboration

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