from demonstrator towards a full-ring brain scanner

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on behalf of the AX-PET collaboration

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The AX-PET collaboration

Extraordinary example of technology transfer from High Energy Physics to Medical Physics.

The goal of the AX-PET collaboration

✔ Build and fully characterize a demonstrator of a PET camera with 3D localization of the gamma interaction point, decoupling spatial resolution from sensitivity.
Different PET detector concepts

<table>
<thead>
<tr>
<th></th>
<th>Small crystals</th>
<th>Big crystals</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>😞</td>
<td>😊</td>
</tr>
<tr>
<td>Resolution</td>
<td>😊</td>
<td>😞</td>
</tr>
</tbody>
</table>

DOI dependence on crystal thickness

- Phoswich scheme
- Different crystals with different decay times
- LSO
- LuYAP

Position-sensitive Avalanche Photodiodes

Monolithic scintillator with pixellated read-out.


1 mm³ crystal
The AX-PET concept

Axially oriented crystals

- x-y discrete design
- Trans-axial resolution $\sigma = \frac{d}{\sqrt{12}}$

Hodoscope of WLS strips placed underneath each crystal layer.

- $N \geq 1$ strips fired per event.
- Minimum resolution in z $\sigma = \frac{w}{\sqrt{12}}$
The AX-PET concept

✔ 3D localization of the gamma interaction with discrete trans-axial coordinate and continuous z.

✔ High resolution with mitigated DOI effect.

✔ Fully scalable design that can be adapted to different scenario requirements.
The AX-PET module

Our choice! Originally conceived for brain imaging.

- 6 layers
- 8 crystals per layer
- 26 WLS strips interleaved to each layer

48 crystals + 156 WLS strips = 204 read-out channels

Alternate individual read-out to guarantee compactness
Staggering of crystals to achieve more homogeneous sampling (smaller gaps)
LYSO crystals (Lu$_{1.8}$Y$_{0.2}$SiO$_5$: Ce) Prelude 420 from Saint Gobain
- 3x3x100 mm$^3$ read-out on one side
- Aluminum coated on the opposite side to enhance reflectivity ~85%
- Intrinsic resolution (8.3 ± 0.5)% FWHM @511 keV

EJ-280-10x from Eljen Technology
- 3x0.9x40 mm$^3$ read-out on one side
- Decay time 8.5 ns
- $\lambda_{\text{blue}} = 0.4$ mm (highly doped 10x) $\lambda_{\text{green}} = 188$ mm

MPPC 3.22×1.19 Octagon–SMD
- 1.2 x 3.2 mm$^2$ active area
- 782 pixels
- custom made units
- ~40% PDE
- ~1000 pe @ 511 keV

MPPC S10362–33–050C
- 3x3 mm$^2$ active area
- 3600 pixels
- ~40% PDE
- ~10-50 pe @ 511 keV in LYSO
The AX-PET demonstrator

Two fully assembled modules at CERN.
DAQ & Readout Electronics
- Individual analogue readout of MPPC output
- External trigger (NIM logic) to sort coincidences
  - Single crystal $E > 50$ keV
  - Module energy $E_{\text{sum}}[400 \text{ keV}, 600 \text{ keV}]

- Scatter in patient rejected
- Inter-Crystal scatter events accepted
Detector calibration and energy resolution

Internal trigger - no source

External trigger - Na\textsubscript{22} source

Lu\textsubscript{176} isotope:
- 250 Bq/crystal
- 202 and 303 keV

1 crystal per module
511 keV

Typical calibration curve

Lu\textsubscript{176} isotope:
• 250 Bq/crystal
• 202 and 303 keV

Energy resolution

\(< \Delta E_{\text{FWHM}} > \sim 11.8\% @511 \text{ keV} \)
(over two modules 96 LYSO crystals)
Axial resolution

Tagging crystal to scan the axial dimension in each module

The two modules in coincidence

Na22 source

Intrinsic axial spatial resolution
Mod 1: 1.75 mm FWHM
Mod 2: 1.83 mm FWHM
(source corrected)

Axial resolution w/ LOR confocal reconstruction
1.35 mm FWHM
(after positron range and a-collinearity correction)
The proof-of-concept

Several measurement campaigns
1) global procedure test

Face-to-face
\( \theta = 0^\circ, 20^\circ, 40^\circ \ldots 360^\circ \) (18 steps)

Apr. 2010 ETH
 Jul. 2010 AAA
 Jul. 2011 AAA
 Apr. 2012 ETH

Thin capillaries
The proof-of-concept

Several measurement campaigns
1) global procedure test
2) extended sources, extended FOV

θ = 0°, 20°, 40°... 360° (18 steps)

Apr. 2010 ETH
Jul. 2010 AAA
Jul. 2011 AAA
Apr. 2012 ETH

Thin capillaries
Micro-Derenzo
Mini-Deluxe
Homogeneous
NEMA
The AX-PET concept

The Demonstrator

Proof-of-concept

Software

Brain Imaging

The proof-of-concept

Several measurement campaigns
1) global procedure test
2) extended sources, extended FOV, fixed time per scan
3) Improved acquisition protocol: multiple scans per acquisition with adjusted acquisition time

θ = 0°, 20°, 40°... 360° (18 steps)

φ = 20°

Apr. 2010
ETH

Jul. 2010
AAA

Jul. 2011
AAA

Apr. 2012
ETH

Thin capillaries

Micro-Derenzo

Mini-Deluxe

Homogeneous

NEMA

P. Solevi

II Symposium on PET
Several measurement campaigns
1) global procedure test
2) extended sources, extended FOV, fixed time per scan
3) Improved acquisition protocol: multiple scans per acquisition with adjusted acquisition time
4) Imaging small animals
The proof-of-concept

1 mm rod reconstructed with 1.6 mm FWHM

- Reconstruction: LOR-Histogram + off-line SM
- $4.2 \times 10^8$ LORs
- Voxel size: $1 \times 1 \times 1 \, \text{mm}^3$
- No corrections
- 100 iterations

Rods parallel to z axis

Rods perpendicular to z axis

Hollow rod diameters

AAA 2011
The proof-of-concept

1 mm rod reconstructed with 1.6 mm FWMH

- Reconstruction: LOR-Histogram + off-line SM
- $4.20 \times 10^8$ LORs
- Voxel size: $1 \times 1 \times 1 \text{ mm}^3$
- No corrections
- 100 iterations

AAA 2011

P. Solevi
Software developments

Challenges (just some of them..)

- Two coordinates with different readouts: continuous z and discrete x-y.
  - List-mode data allows to preserve spatial resolution, no binning is required.

- Prototype in continuos evolution: different acquisition protocols, FOV varies.
  - System Response Matrix calculation required in ML-EM reconstruction: off-line (more accurate, computationally consuming) and on-the-fly (less accurate but better deals with prototype evolution).

- Novel device with features that require dedicated reconstruction approaches.
  - Inter-Crystal Scatter events: it has the potential to enhance sensitivity but resolution shall be preserved.

- Monte Carlo support is required to support the prototype predictions and developments, test reconstruction SW, bring some light on measurements understanding.
  - Common tool such as GATE can’t model such a complex system, dedicated Monte Carlo model is required.
The gamma undergoes multiple Compton interactions within the module (~30%)

- We can’t access the true kinematics of the event.
- How to deal with it at reconstruction level?
Software developments: ICS Inclusion

Conventional approach
- Selection: selecting one of the two LORs by probability criteria
- Low identification success rate (~70% so far with NN)

Proposed approach
- Reconstruct both LORs that is preserving the full probability function associated to the V-shape.

\[
\begin{align*}
    a &= a_1 \text{ if } w_1 > w_2 \\
    a &= a_2 \text{ if } w_2 > w_1 \\
    a_1, a_2: \quad a &= w_1 a_1 + w_2 a_2
\end{align*}
\]
Software developments: ICS Inclusion

Selection

Golden-reference image

V-proj

Inclusion

AAA 2011

J.E. Gillam et al, PMB 59(2014)
General considerations

- Sensitivity increases in all imaged subjects.
- SNR improves but not as much as sensitivity.
- Increase in noisy counts in cold regions (see NEMA) is mitigated by the inclusion approach than other conventional ICS treatments.

ETH 2012

J.E. Gillam et al, PMB 59(2014)
Dedicated Monte Carlo model based on GATE classes.

- Geometry of the detector (staggering, layered, etc.)
- WLS response model: it has to be computationally efficient therefore an analytical model of the signal on the strips is tuned on experimental data from dedicated experimental set-ups.
- Intrinsic radioactivity
- Dedicated coincidence sorter: WLS channels shall be treated as well, hybrid dead-time model, etc.

P. Solevi et al, PMB 58(2013)
AX-PET for brain imaging

- AX-PET was at the very beginning conceived for Brain Imaging (3x3 mm$^2$ crystal cross section, high axial resolution, etc).

Demonstrator design
- 48 modules arranged over a ring of 468 mm diameter.
- Electronics performance improved (within a realistic technological horizon):
  - 75 ns integration time window (pile-up)
  - [400,650] keV @ module
  - 5 ns coincidence window
  - Improved dead-time at DAQ level

Can we do better?
AX-PET for brain imaging

- AX-PET was at the very beginning conceived for Brain Imaging (3x3 mm² crystal cross section, high axial resolution, etc).
AX-PET for brain imaging

- AX-PET was at the very beginning conceived for Brain Imaging (3x3 mm$^2$ crystal cross section, high axial resolution, etc).

Novel design
- 20 degrees slanted layers.
- 300 layers arranged over a ring of 474 mm diameter.
- One module is the sum of 6 continuous layers.
AX-PET was at the very beginning conceived for Brain Imaging (3x3 mm$^2$ crystal cross section, high axial resolution, etc).
• The two geometries are comparable in terms of sensitivity.
• Reduced gaps translates into a more homogeneous sampling over the FOV.
Cologne phantom

Resolution phantom

- 219 mm diameter lucite disk, 28 mm thick.
- Different rods of different diameters (2, 3 and 4 mm with 4, 6 and 8 mm pitch).
- 60 MBq activity in the phantom (close to NEC peak).

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<th>Novel</th>
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Images at iteration 10, 5subLORs, no attenuation correction.
Cologne phantom

Resolution phantom

- Standard Golden
- Novel Golden
- Standard Golden + ICS
- Novel Golden + ICS
NEMA phantom

**Image quality phantom**

- 200 mm diameter air disk, 60 mm thick.
- Different rods (50 mm Hot-Cold, 4 mm Hot-Cold) in homogeneous background.
- Different activity ratios studied: 1.2:1, 5:1 and 20:1.
- 26 MBq total activity at the different ratios.

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NEMA phantom

Image quality phantom

5:1 ratio

20:1 ratio

Iteration 10, 5 subLORs, random rejected.
The collaboration accomplished with the primary objective:
  • two modules built and fully characterized.

What we learned from simple source laboratory set-ups?
  • spatial resolution 2 mm (x-y) and 1.35 mm (z).
  • energy resolution 11.8% FWHM @ 511 keV.
  • 3D localization of the gamma interaction.
  • Large Compton Scatter fraction ~30%.

And from phantom measurements?
  • AX-PET nicely works with extended sources and small animals, too.
  • That every improvement in hardware has to be followed by at least the same effort in software development (Monte Carlo, new reconstruction algorithms) and usually it pays off.

AX-PET for brain imaging?
  • Preliminary Monte Carlo studies are promising.
  • Exquisite example of the AX-PET scalability.
Thanks for your attention!
Brain imaging challenges

- **Oncology**: brain tumors have 0.1% prevalence in western population, but among the most fatal cancers (malignant gliomas ~70%).
  - F18-FDG commonly used tracer, contrast can range from large necrotic tumor core lesion to low contrast small regions.
  - Tumors follow-up is usually characterized by SUV (~Activity concentration/Injected dose) which is affected by RC and PVE, for lesions below few times the system resolution.
  - The higher the resolution the better SUV is estimated.

- **Impairment Dementia**: life expectancy increases and with it dementia (WHO predict 48 million people in 2040 affected by dementia, AD mostly).
  - There is a huge variety of contrasts and lesion sizes related to AD.
  - Sensitivity is crucial to detect small lesions at early stages when treatments are still possible.
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
System matrix element

\[ n_{j}^{k+1} = \frac{n_{j}^{k}}{\sum_{i=0}^{1} a_{i,j} \sum_{i \in M} \sum_{j=0}^{J} a_{i,j} n_{j}^{k}} \]

Sensitivity or normalization \( s_{j} \)

Image at iteration \( k \)

And what if \( a_{ij} \) is a Triple \( a_{i'j} \) ?

Conventional approach \( \rightarrow \) Identification

\[
\frac{a_{i'j}}{\sum_{j=0}^{J} a_{i'j} n_{j}^{k}} = \frac{a_{i,j}}{\sum_{j=0}^{J} a_{i,j} n_{j}^{k}}
\]

- One of the 2 LOR is selected, \( (t = 1 \text{ or } 2) \).
- In this study, randomized selection is used.

Our approach \( \rightarrow \) V-projection

\[
a_{i'j} = \eta_{1} a_{i1j} + \eta_{2} a_{i2j}
\]

- Both LORs are kept but weights are assigned.
- In this study, \( \eta_{t} = 0.5 \) equivalent to randomized selection.