Usage of long axially oriented crystals for PET applications: the AX-PET Demonstrator and beyond

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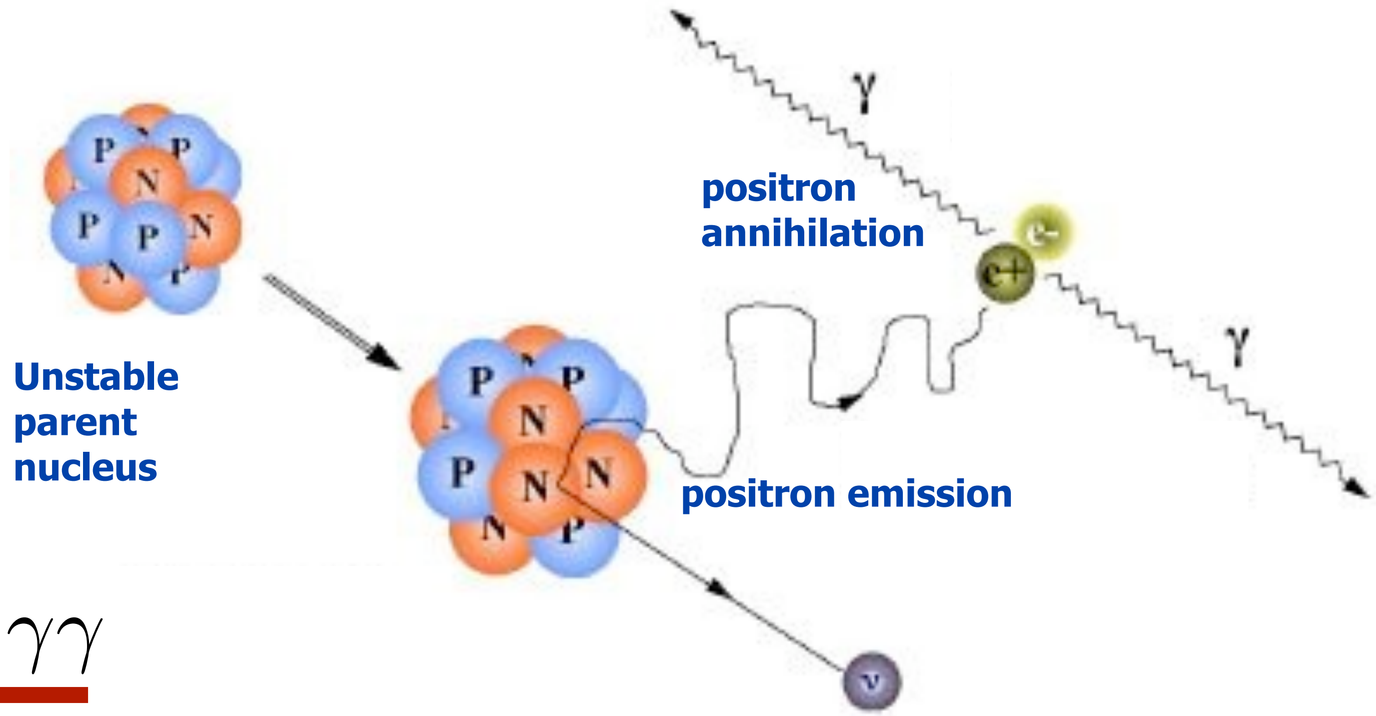
Outline

- **Brief introduction about Positron Emission Tomography (PET)**
- **Long axially oriented crystals** :
  What is it ? Why?
- **The AX-PET Demonstrator**
  Fully operational demonstrator for a PET scanner
  Detector concepts
  AX-PET modules
  AX-PET performance
  Simulations
  Tomographic image reconstruction (phantoms and small animals)
- **Studies of long axial crystals readout with digital Si-PM**
  Timing performance
  Axial resolution
- **Conclusions**

Positron Emission and Annihilation

- basis of the PET system **Positron Emission :** $p \rightarrow n + e^+ + \nu_e$
- β^+ decay of different radionuclides

Radionuclide	Half life	Emax_e+(MeV)
^{11}C	20.4 min	0,96
^{15}O	122 sec	1,73
^{18}F	109,8 min	0,63
^{22}Na	2.6 years	0,55



- **Positron Annihilation :** $e^+e^- \rightarrow \gamma\gamma$
  2 photons emitted
  - "back - to - back"
  - Eγ = 511 keV

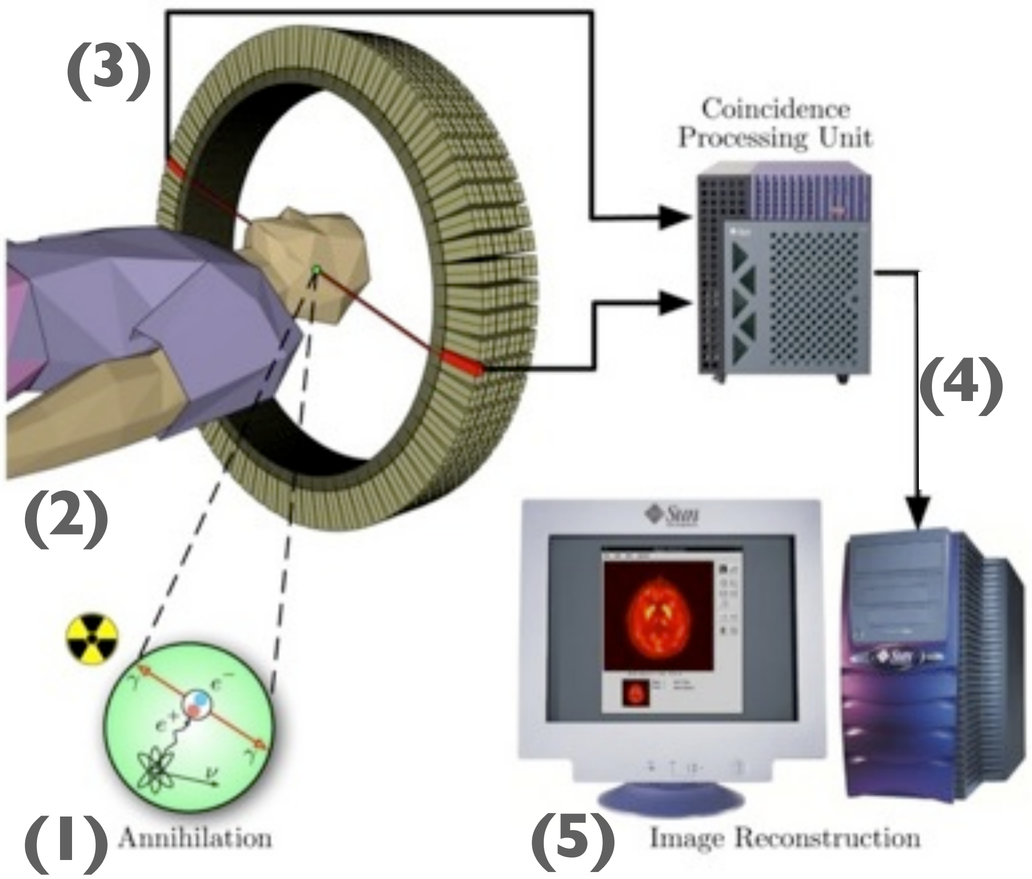
Physics of the positron annihilation => fundamental limits to the PET spatial resolution

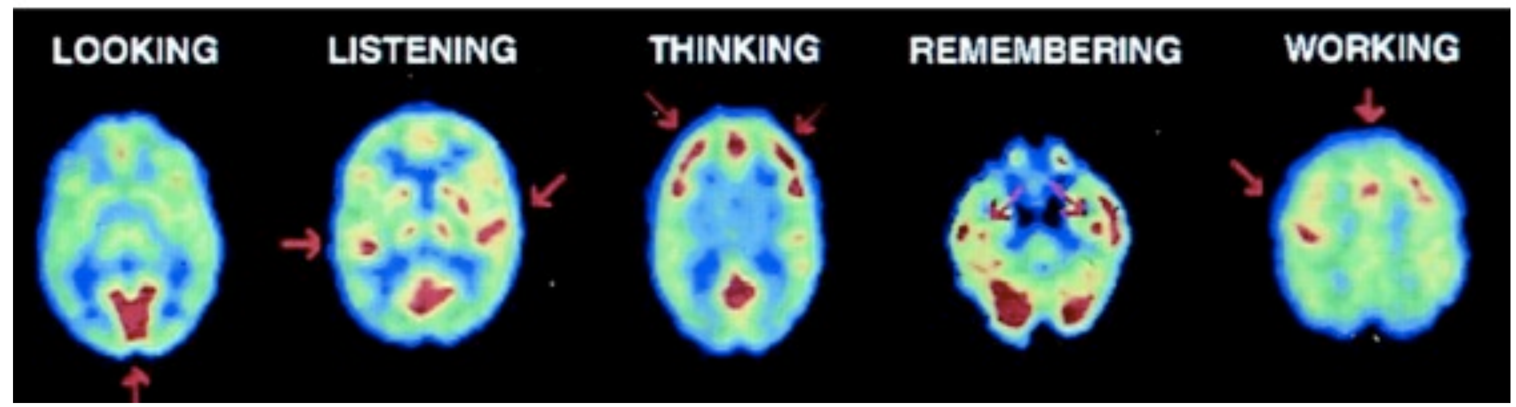
- **Finite positron range (ρ)**
  annihilation position ≠ emission point
  ρ depends on the energy of the positron (i.e. on the radioisotope)
- **Non-collinearity of the 2 photons**
  residual momentum of the e+e- at the annihilation
  the 2 photons are emitted with a small deviation from 180° (Δθ ~ 0.5°)
  blurring of the spatial resolution R_FWHM ~ 0.0022 x D [mm]

Positron Emission Tomography (PET): What is this ?

PET : nuclear imaging technique for “in-vivo” functional imaging

routinely adopted :
- clinical applications (e.g. tumor diagnosis, neuroscience...)
- preclinical (i.e. small animals) applications (e.g. cancer research, tracers developments, pharmacology kinetics...)





A.Del Guerra, CERN Academic Training 2009

radiotracer : positron emitter labelled molecule

(1) Inject the **radiotracer into the body**

(2) Wait for uptaking period

(3) Start the acquisition (i.e. **detection of coinc. events**)

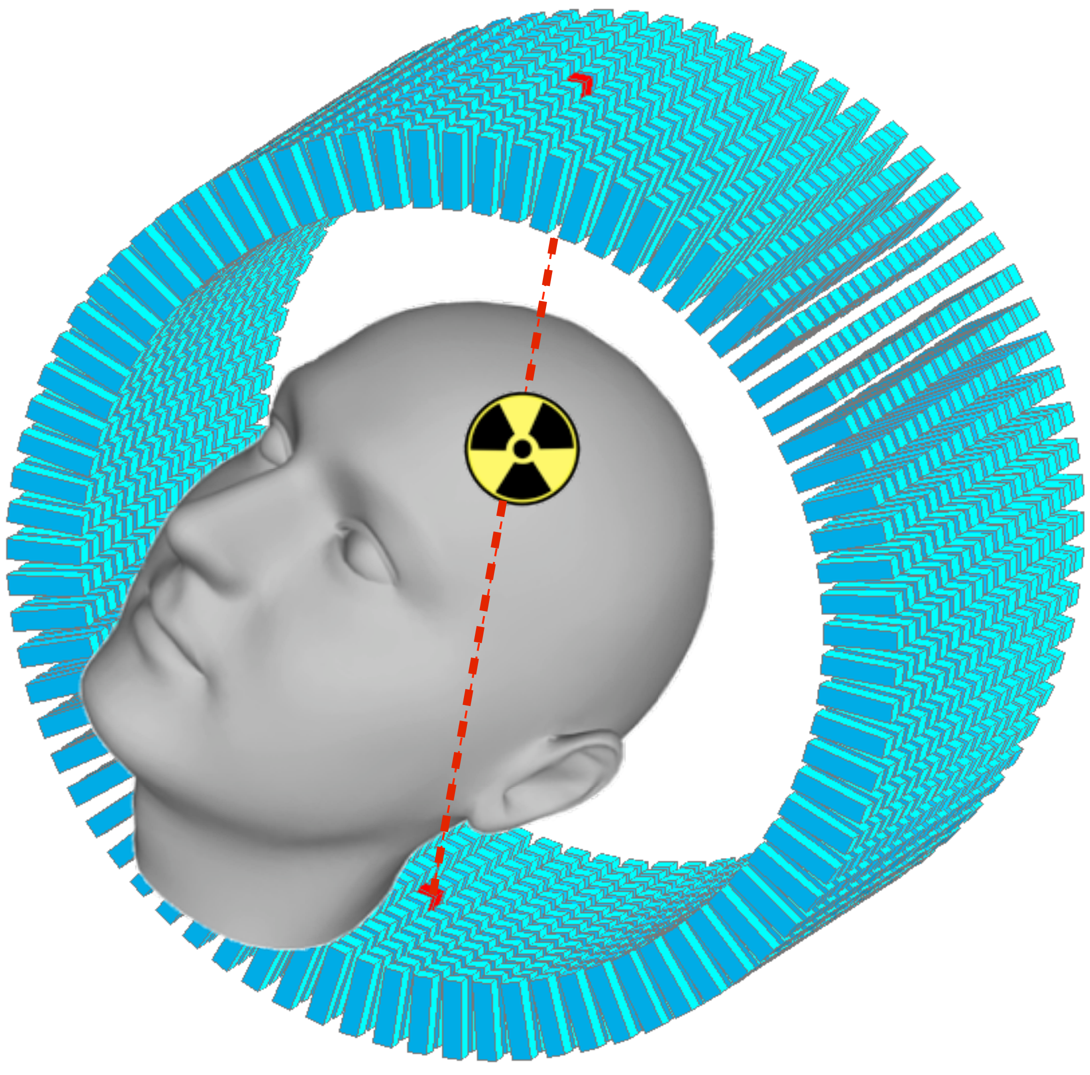
(4) Feed the data into the reconstruction algorithms

(5) **image** of the **activity concentration**

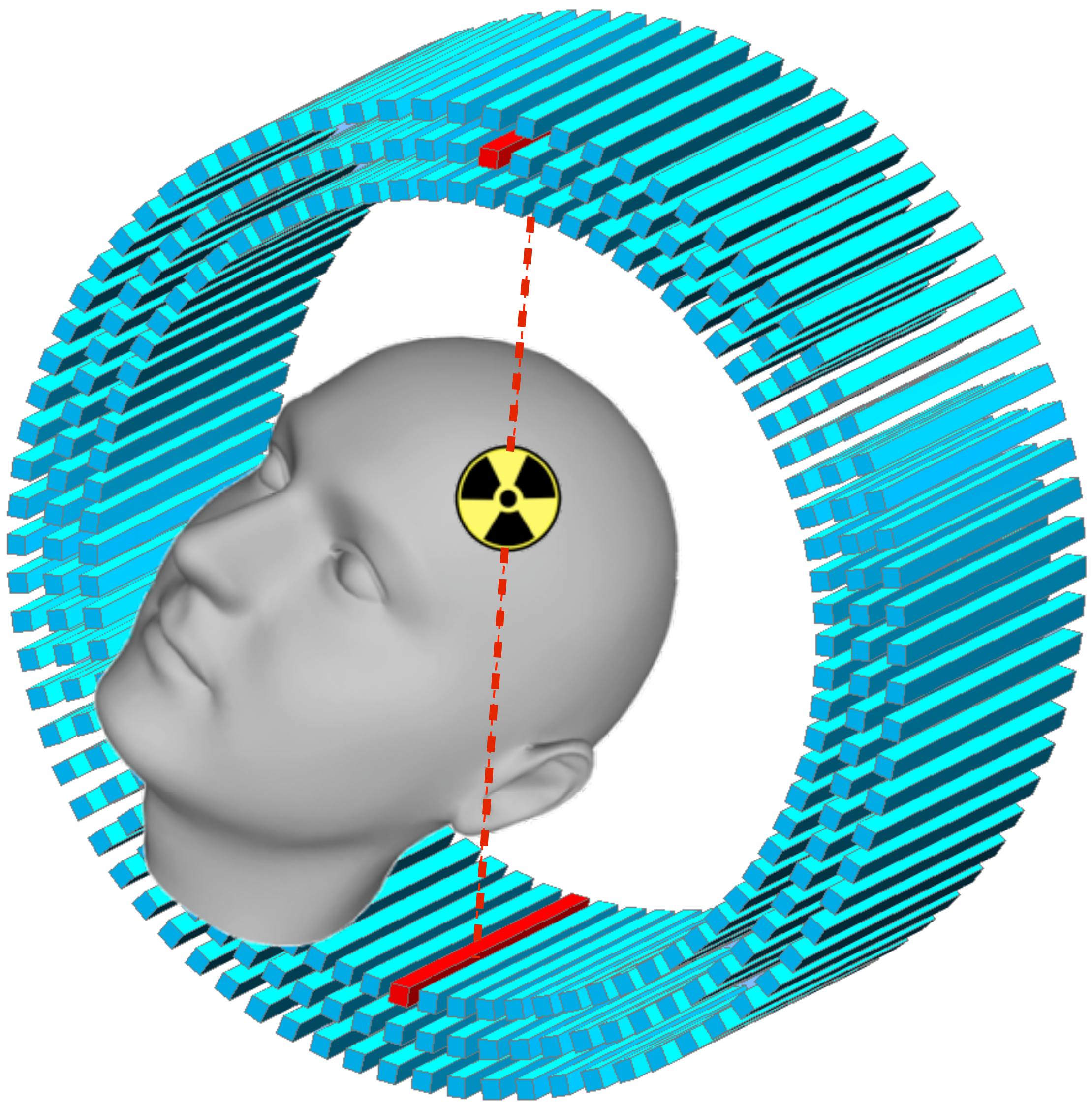
PET detector principle : detection of several 2-γ coincidences

Axial arrangement of crystals in a PET

Conventional radial arrangement



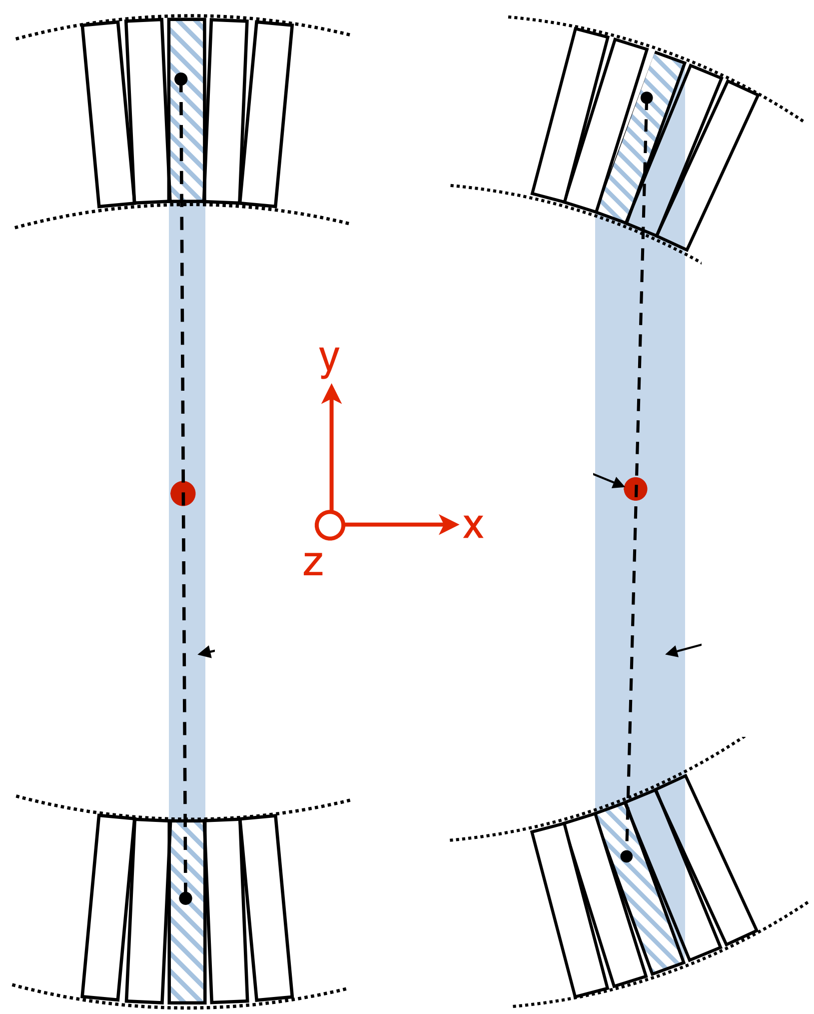
Novel AXIAL arrangement



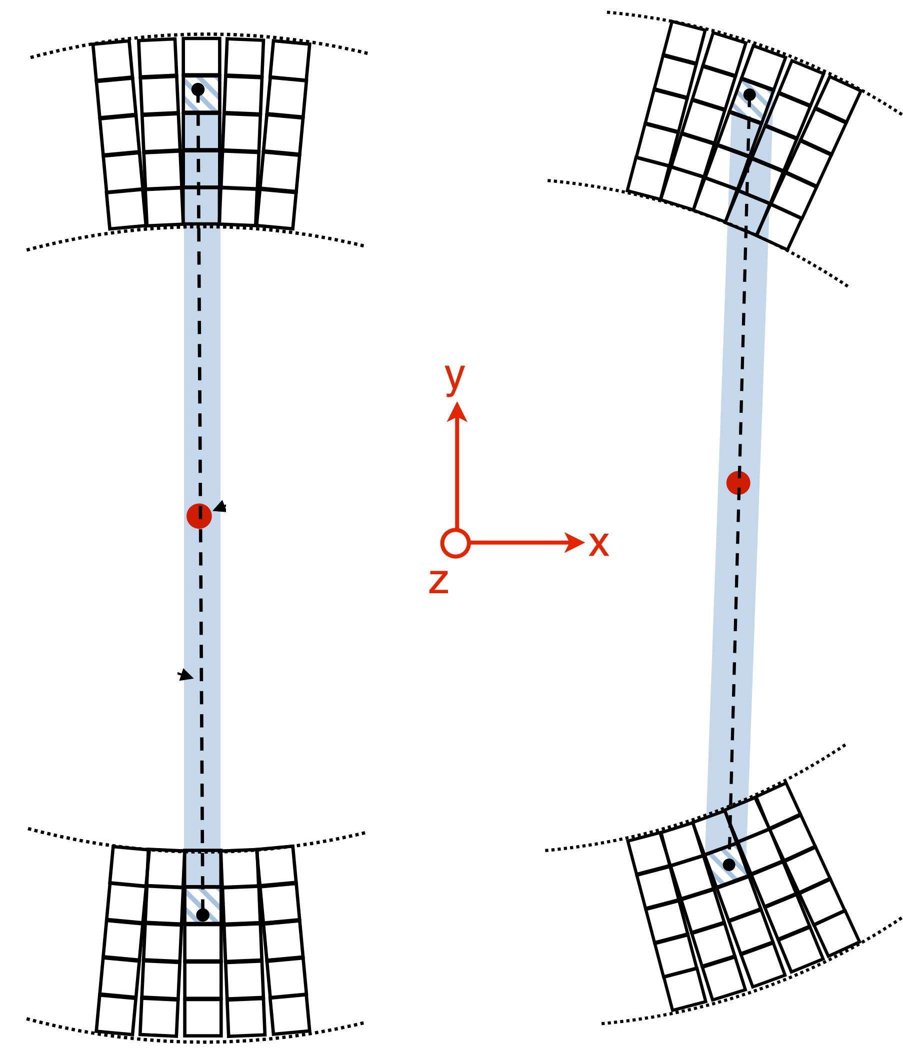
Which is the advantage of axially oriented crystals?

Axial arrangement of crystals in a PET

Conventional radial arrangement



Novel AXIAL arrangement

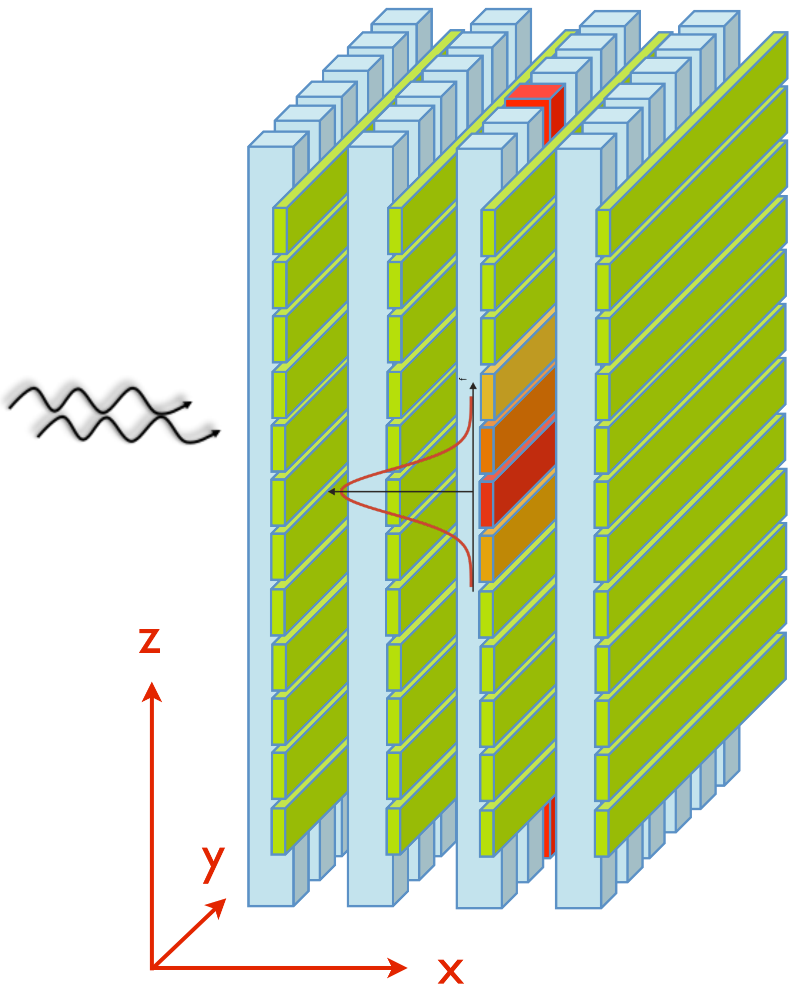


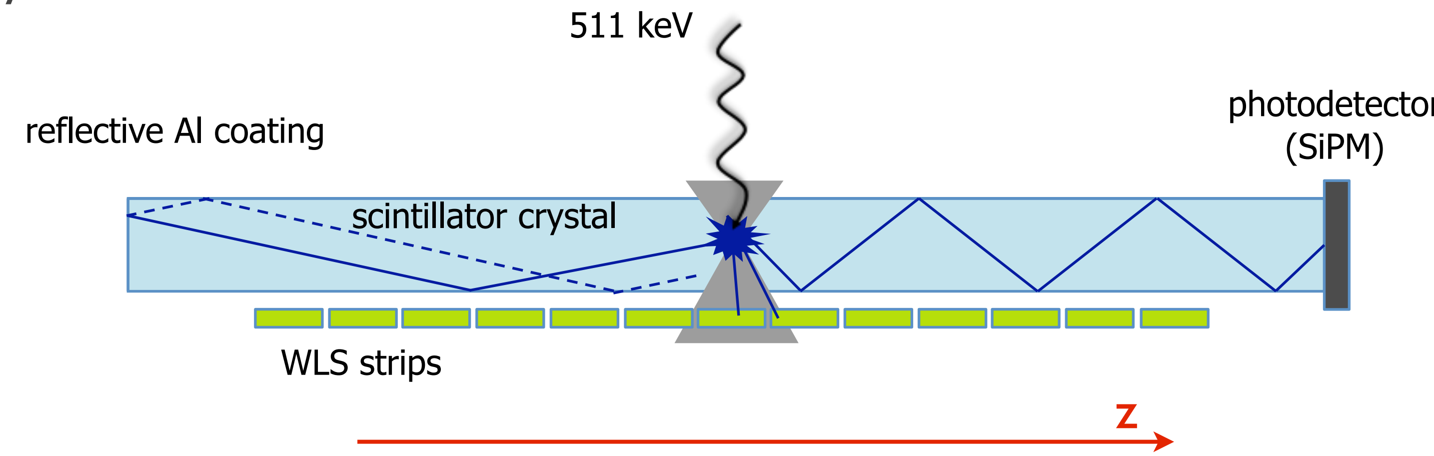
- parallax error
- compromise between spatial resolution and sensitivity (length of the crystal)
- Depth Of Interaction (DOI) techniques required

- sensitivity <=> nr of layers
- spatial resolution <=> crystal cross-sectional(x,y) size
- decoupled sensitivity and resolution
- need to define the axial(z) coordinate

The AX-PET detector concept : Axial coordinate definition

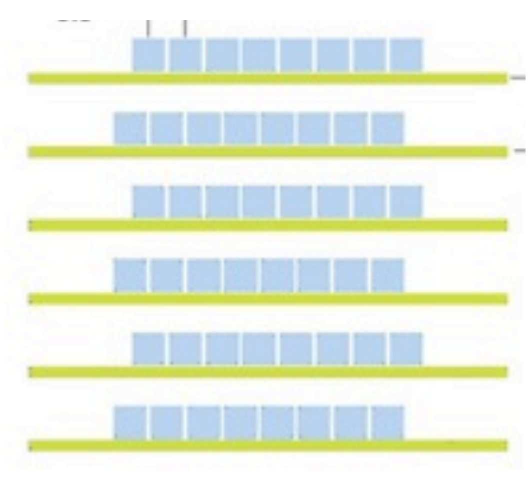
- AX-PET : axial coordinate definition using **arrays of Wave-Length Shifting** (**WLS**) **Strips**
- technique from calorimetry in High Energy Physics





- WLS strips to detect the scintillation light that escapes the crystal corresponding to the interaction point.
- few WLS interested by the event
  <N_strips> ~ 3
  measured total light yield ~ 100 pe
- center of gravity (CoG) => z (axial) coordinate

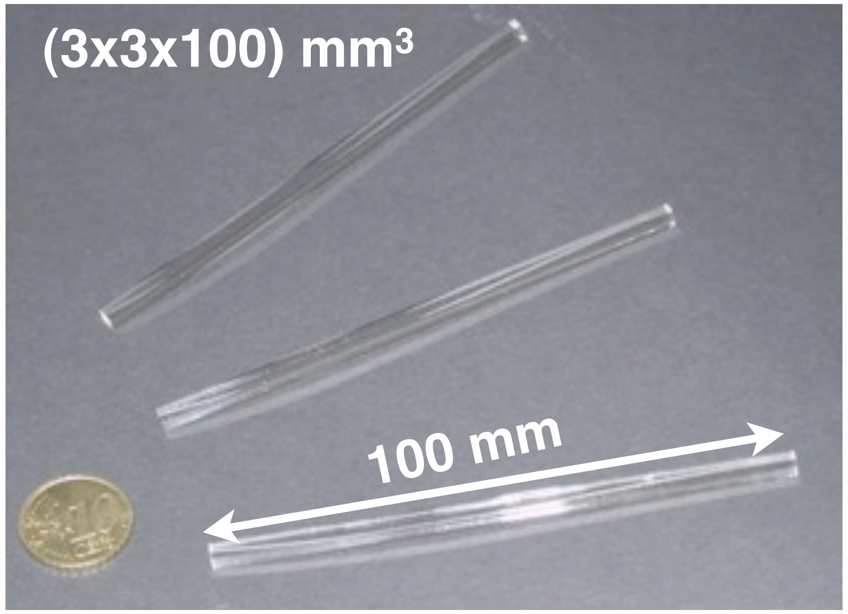
- AX-PET detector : **matrix of staggered layers of scintillator crystals and WLS strips arrays**
- crystals and WLS strips
  => **3D localization of the photon interaction point**
  crystal position => (x,y) ; WLS CoG => z
- crystals => **energy measurement** (small scale calorimeter)



Choice of detector elements

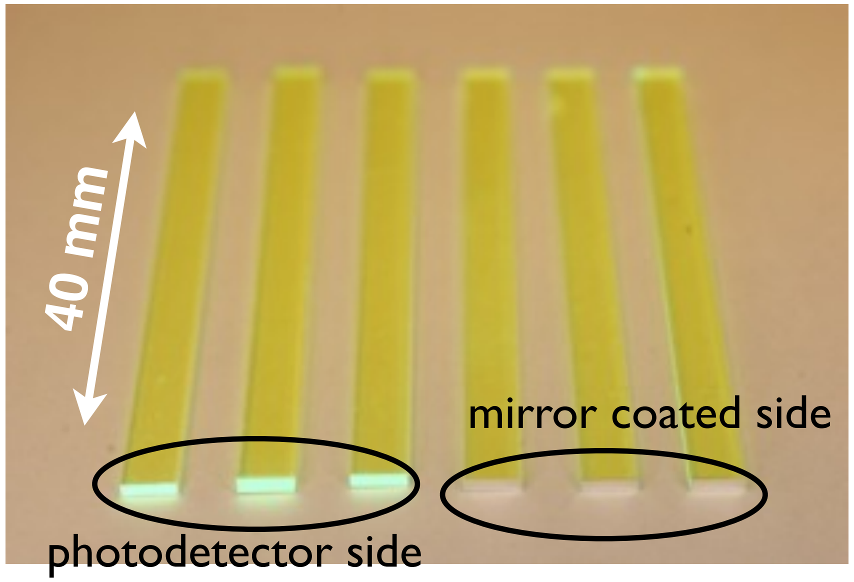
SCINTILLATOR CRYSTALS :

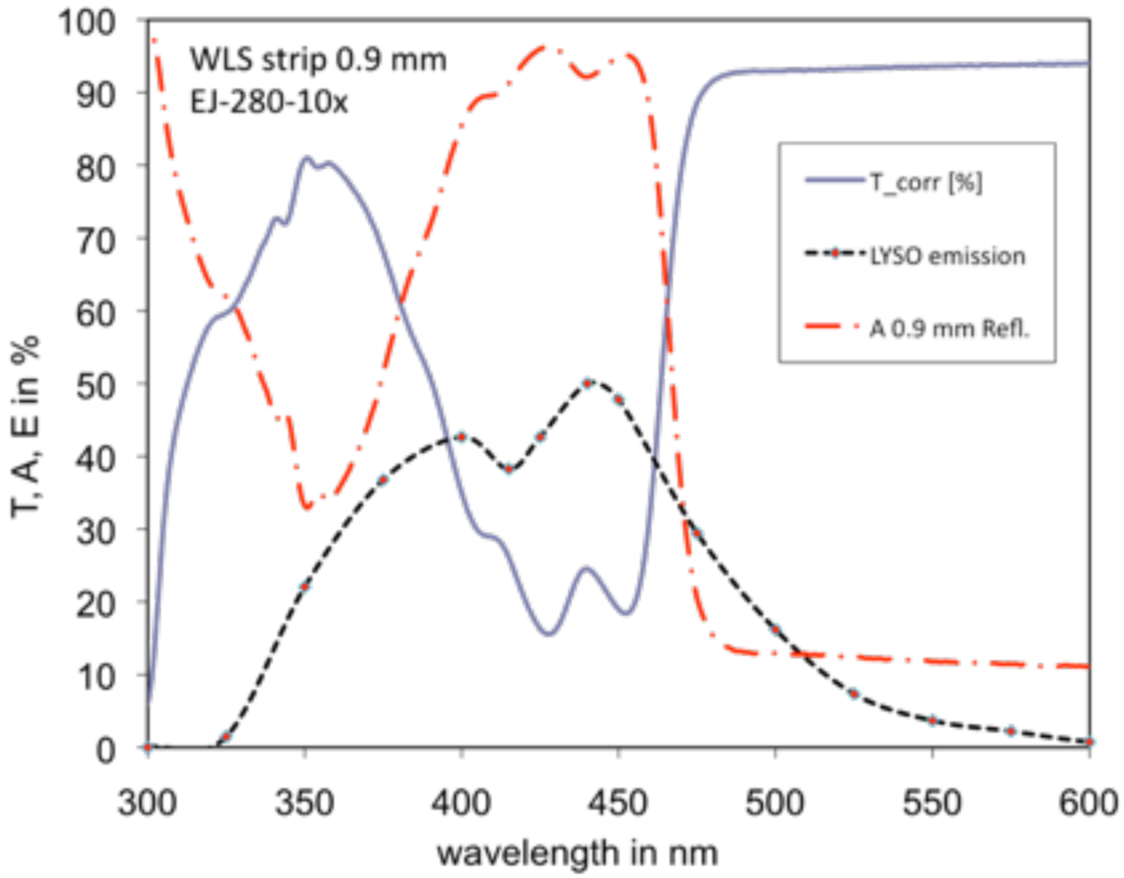
- Inorganic **LYSO** (**$Lu_{1.8}Y_{0.2}SiO_5$: Ce**, Prelude 420 Saint Gobain) **crystals**
  - high atomic number (Z_Lu = 71)
  - high density (ρ = 7.1 g/cm^3)
  - quick decay time (τ = 41 ns)
  - high light yield (32000 γ / MeV)
  - λ @511 keV ~ 1.2 cm
  - non hygroscopic
- **3 x 3 x 100 mm³**



WAVE LENGTH SHIFTING STRIPS (WLS) :

- ELJEN EJ-280-10x
- highly doped (x10 compared to standard) to optimize absorption
- λ_optical = (188 +/- 36) mm [measured!]
- **0.9 x 3 x 40 mm³**



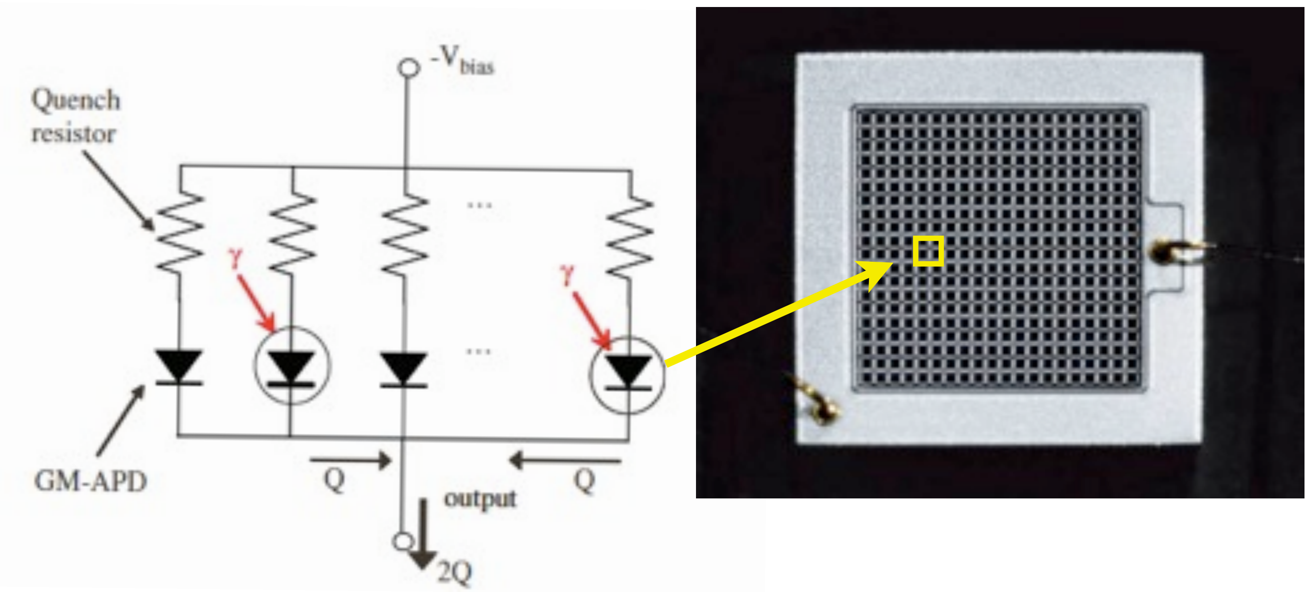


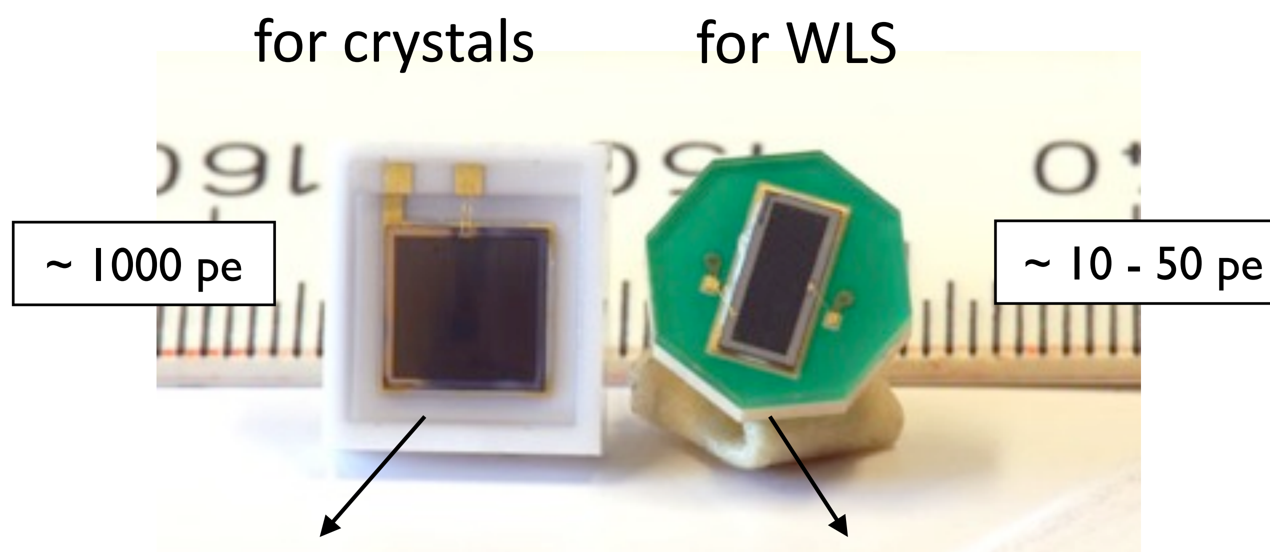
Photodetectors

Each LYSO crystal and WLS strip is individually readout by its own photodetector (1:1 coupling)

Silicon Photomultipliers (SiPM) :

- array of commonly biased APD used in Geiger mode
- output : analogue sum of all the firing APD cells





MPPC S10362-33-050C :
- 3x3 mm^2 active area
- 50 µm x 50 µm pixel
- 3600 pixels

MPPC 3.22×1.19 Octagon-SMD :
- 1.2 x 3.2 mm^2 active area
- 70 µm x 70 µm pixel
- 782 pixels
- custom made units

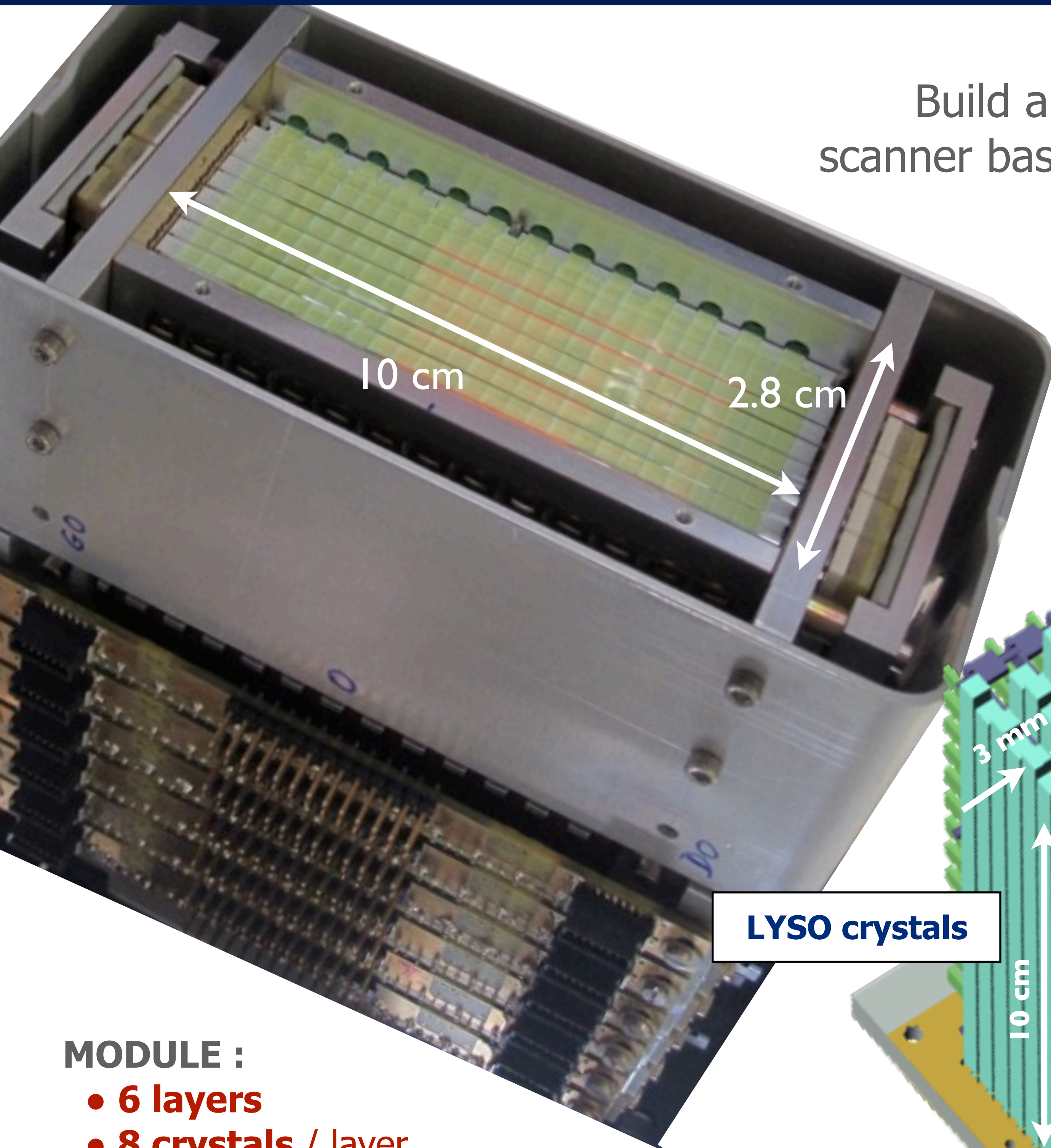
- excellent photon counting capabilities √
- high gain (10^5 to 10^6) at low bias V (~ 70 V) √
- advantages of a Si sensor:
  - high QE √
  - compactness √
  - insensitive to magnetic field (MRI comp.) √
- temperature dependent √
- dark rate (~ 1 MHz @ thr = 0.5 pe) √

	crystal MPPC	WLS MPPC
type	S10362-33-050c	custom tailored
charge gain G	$6 \cdot 10^5$	$1 \cdot 10^6$
dG/dV	$55 \cdot 10^4$ V^{-1}	$110 \cdot 10^4$ 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

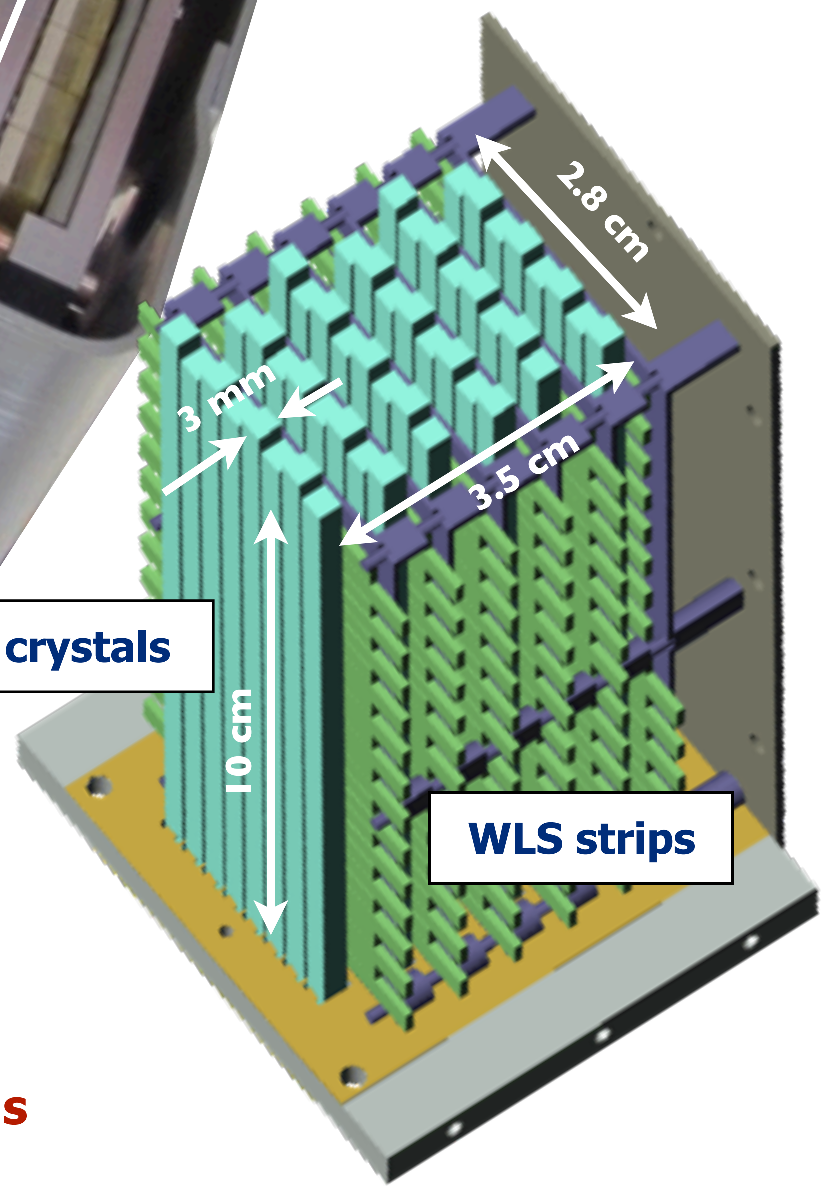
The AX-PET Demonstrator



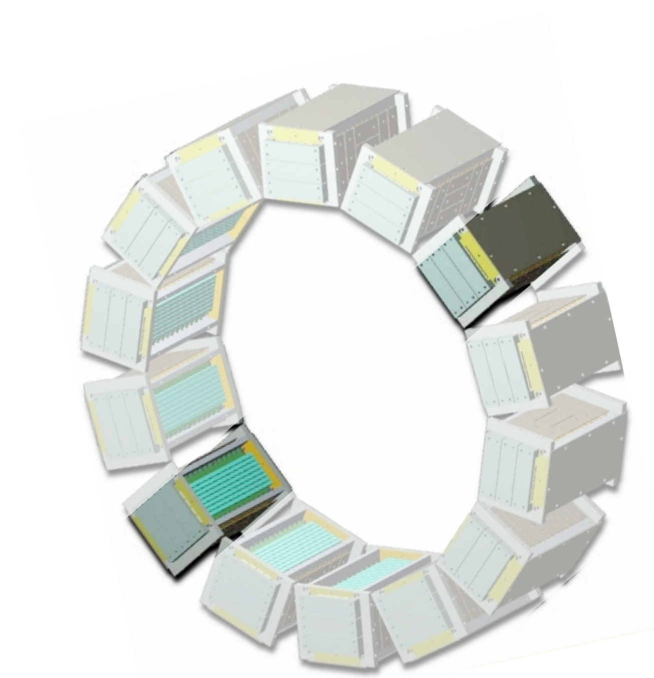
Goal of the collaboration:

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

Demonstrator : Two identical AX-PET modules, operated in coincidence.



x2 ⇒



MODULE :

- **6 layers**
- **8 crystals** / layer
- **26 WLS** / layer
- 48 crystals + 156 WLS = **204 channels**
- all channels **individually readout by SiPMs**

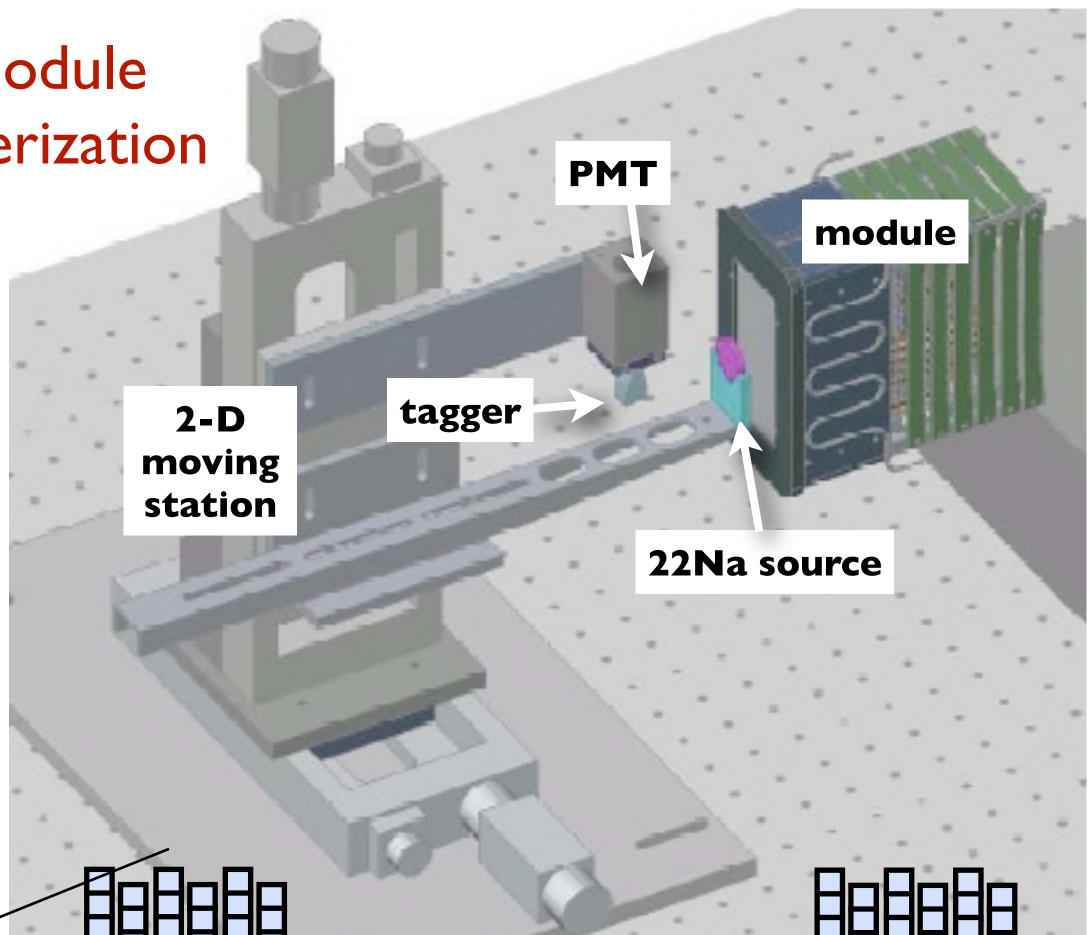
AX-PET Detector performance

- characterization measurements
  - individual module characterization (+ tagging crystal)
  - two-modules coincidence characterization

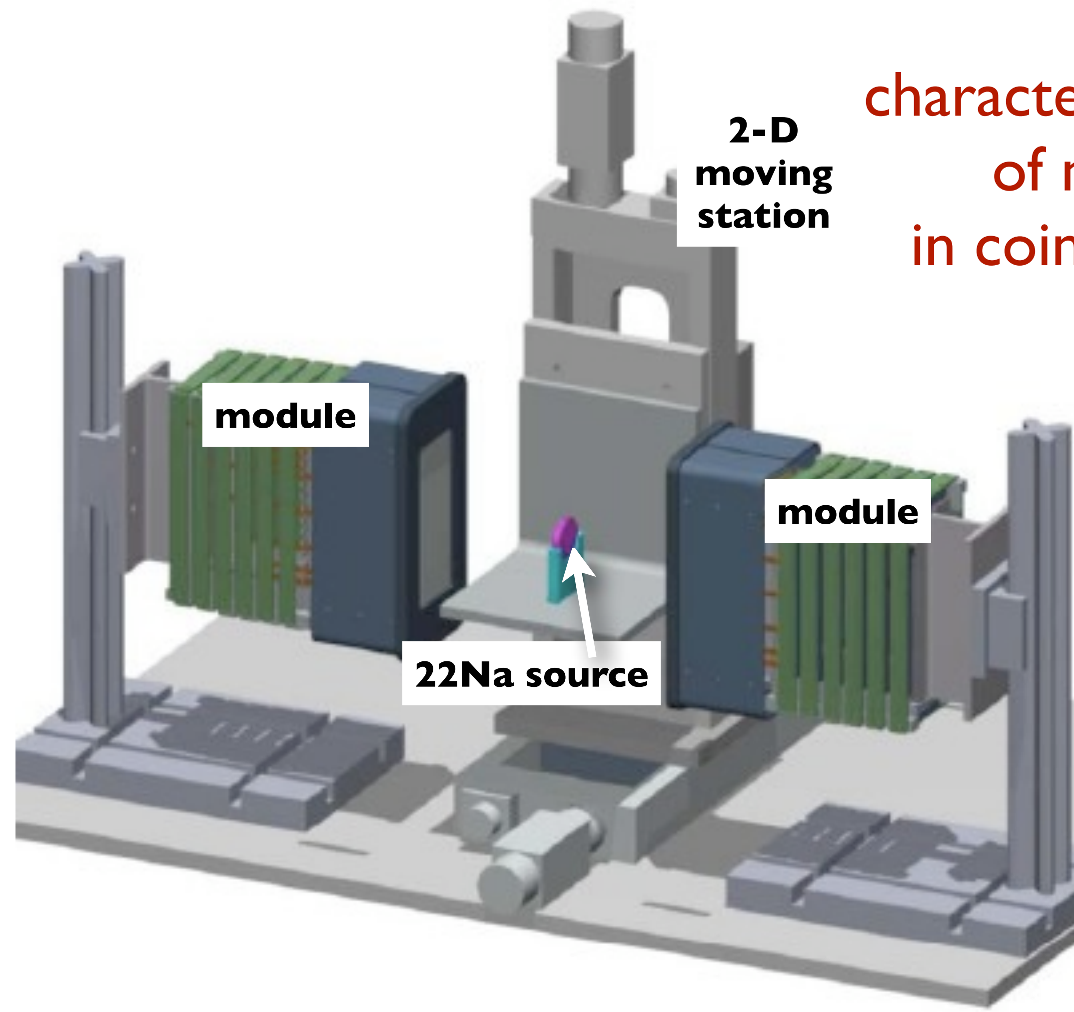
Methods and results :
P. Beltrame et al, NIM A 654 (2011) 546-559

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

single module characterization



characterization of modules in coincidence

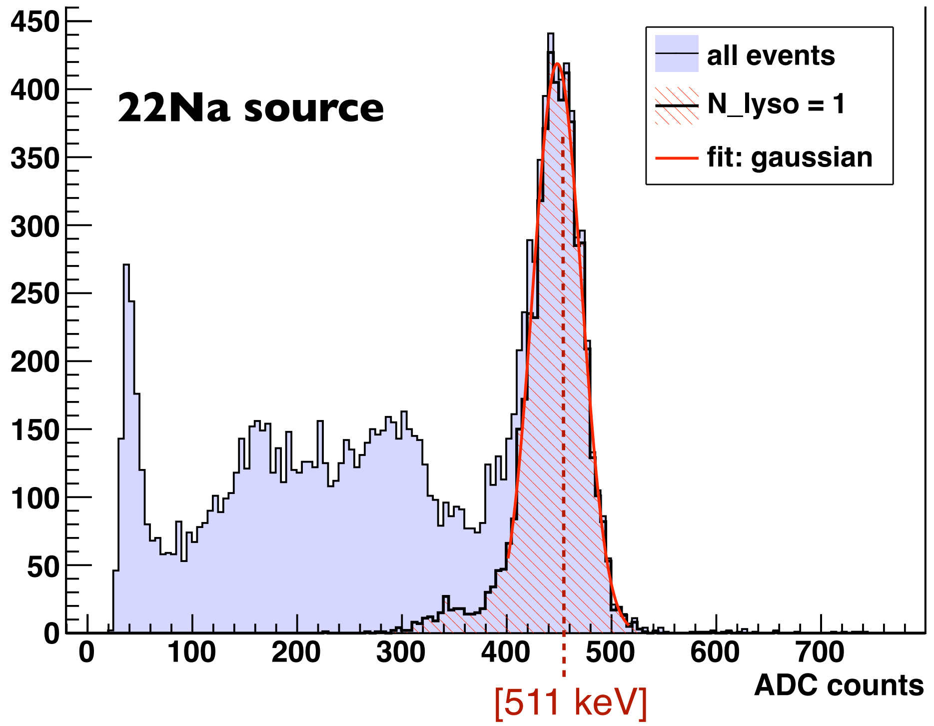


- two different taggers
- different distances tagger / source / module

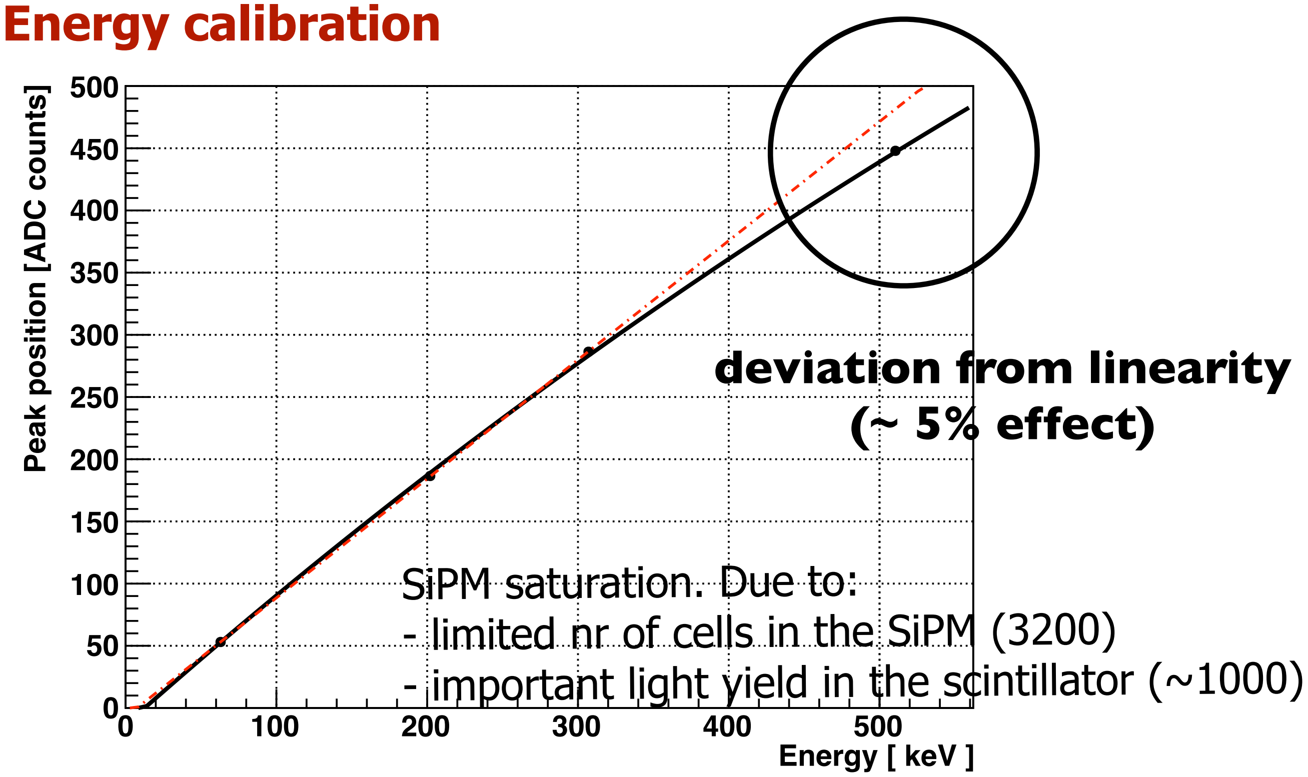
=> both uniform illumination of the module and precisely collimated beam spot

Energy spectra and resolution

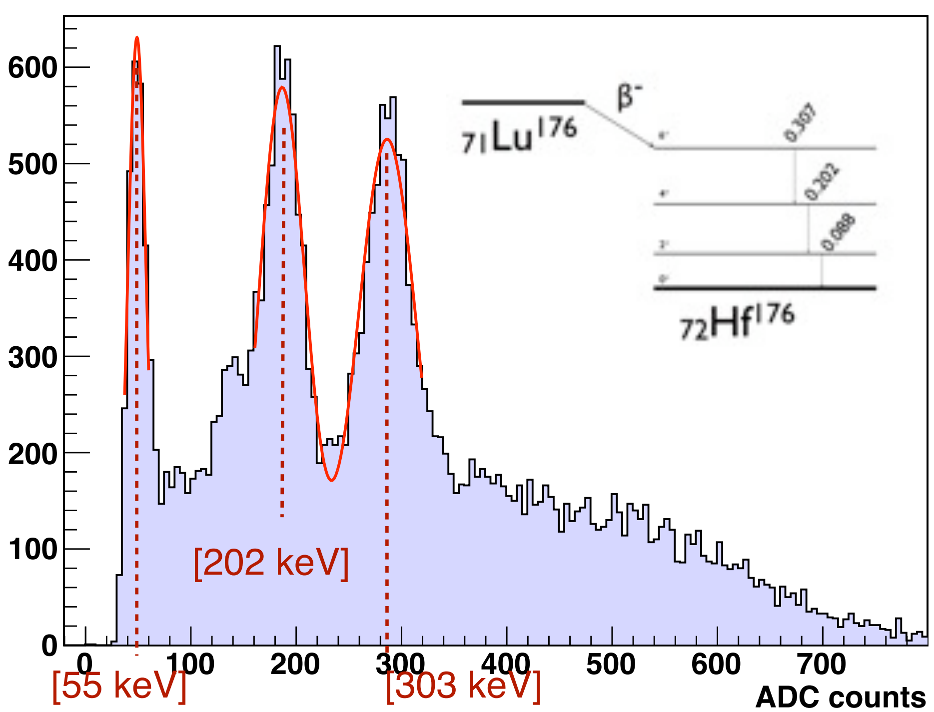
one LYSO crystal, typical Energy spectrum (^{22}Na)



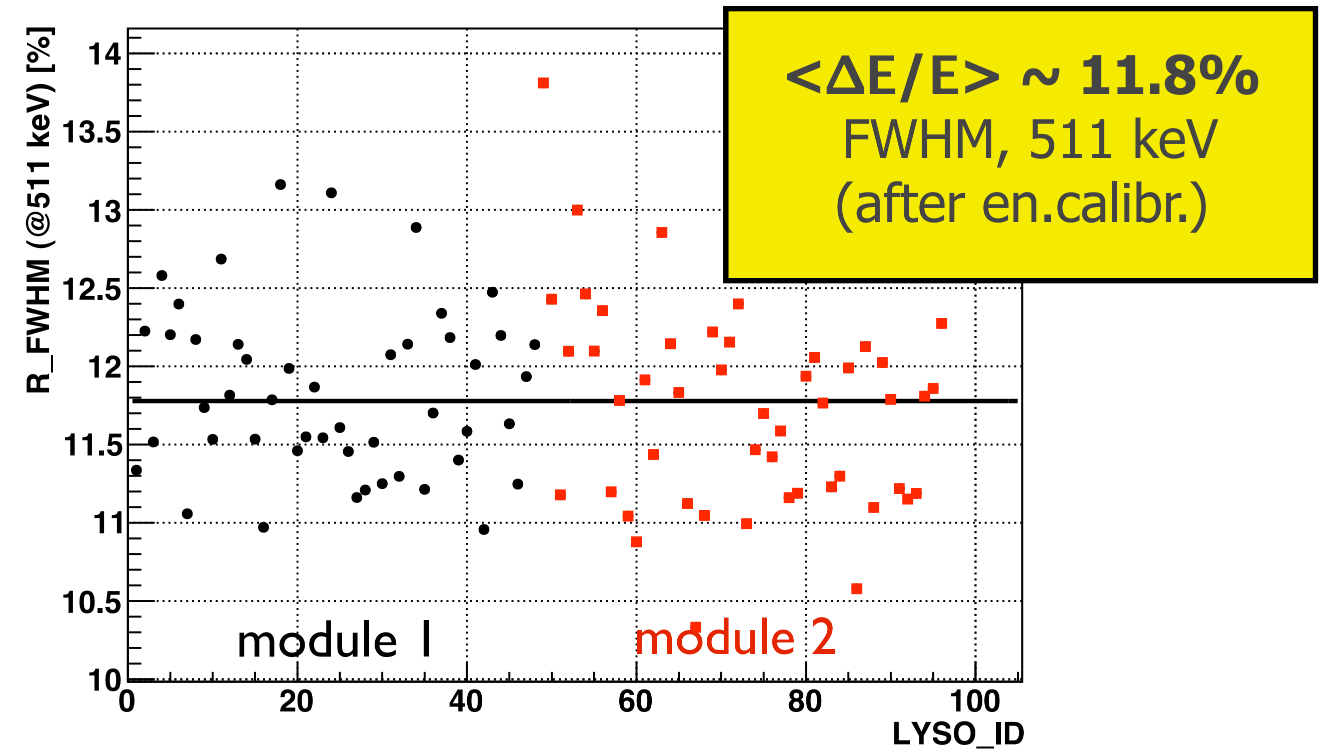
Energy calibration



one LYSO crystal, no source, intrinsic radioactivity



Energy resolution



Spatial resolution

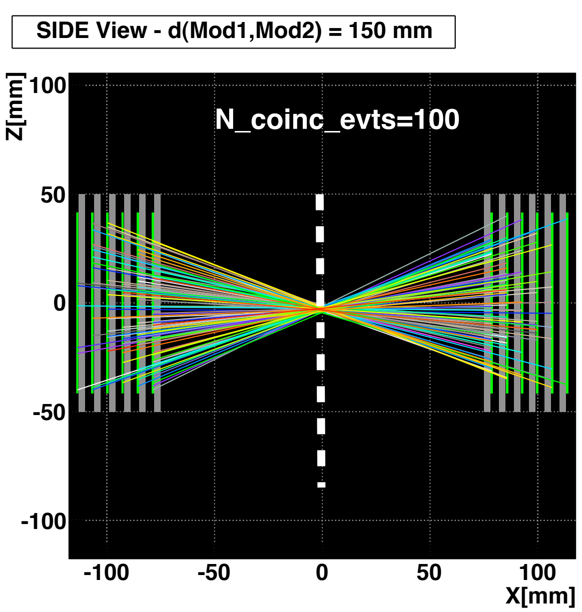
1. **trans-axial direction** : digital, from crystal size

$R_{x,y}$= (3mm/√12)x2.35 ~ 2 mm FWHM => R_{2mods} ~ $R_{x,y}/\sqrt{2}$ **≈ 1.44 mm, FWHM**

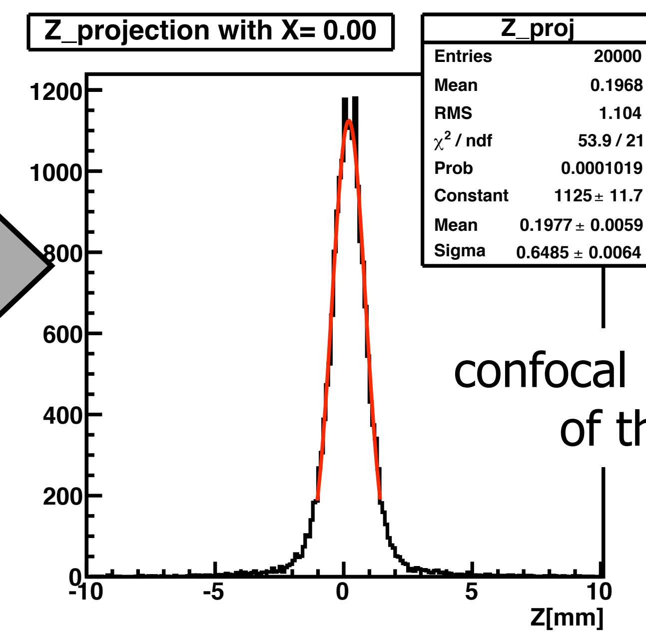
two modules coincidence

2. **axial direction** (two detector coincidences) :

axial coordinate : from center of gravity method (continuous distribution)



Intersection of the LOR with the central plane.

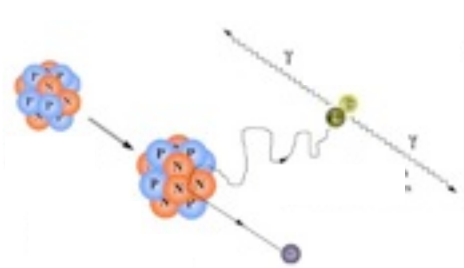


confocal reconstruction of the source

$$R_{intr} = \sqrt{R^2_{meas} - R^2_{\rho} - R^2_{180}}$$

≈ 1.35 mm, FWHM

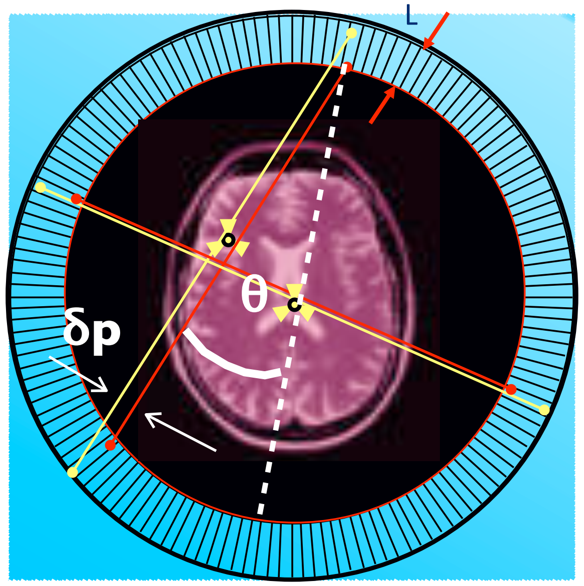
two modules coincidence



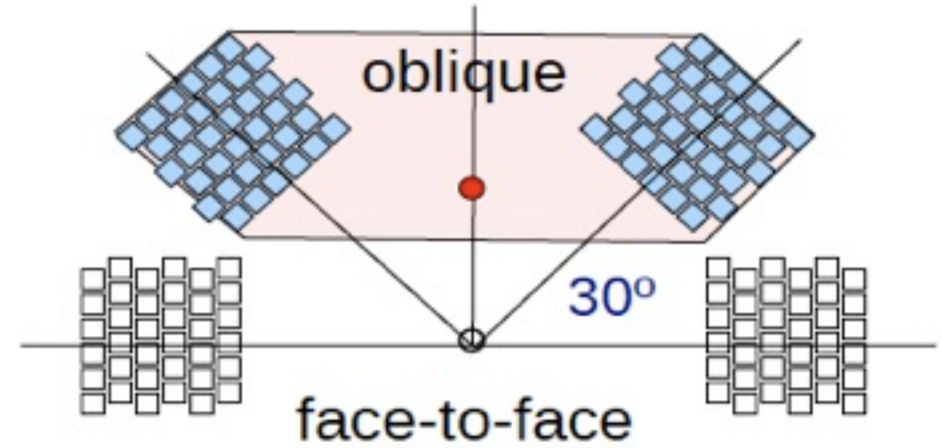
limits to the achievable spatial resolution in a PET system, due to the **physics of positron emission** :

- **positron range** : $R_{\rho}{}^2$ = [0.54 mm]^2
- **non collinearity** : $R_{180}{}^2$ = [0.0022 x Diameter]^2 = [0.33 mm]^2

Parallax free demonstration



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

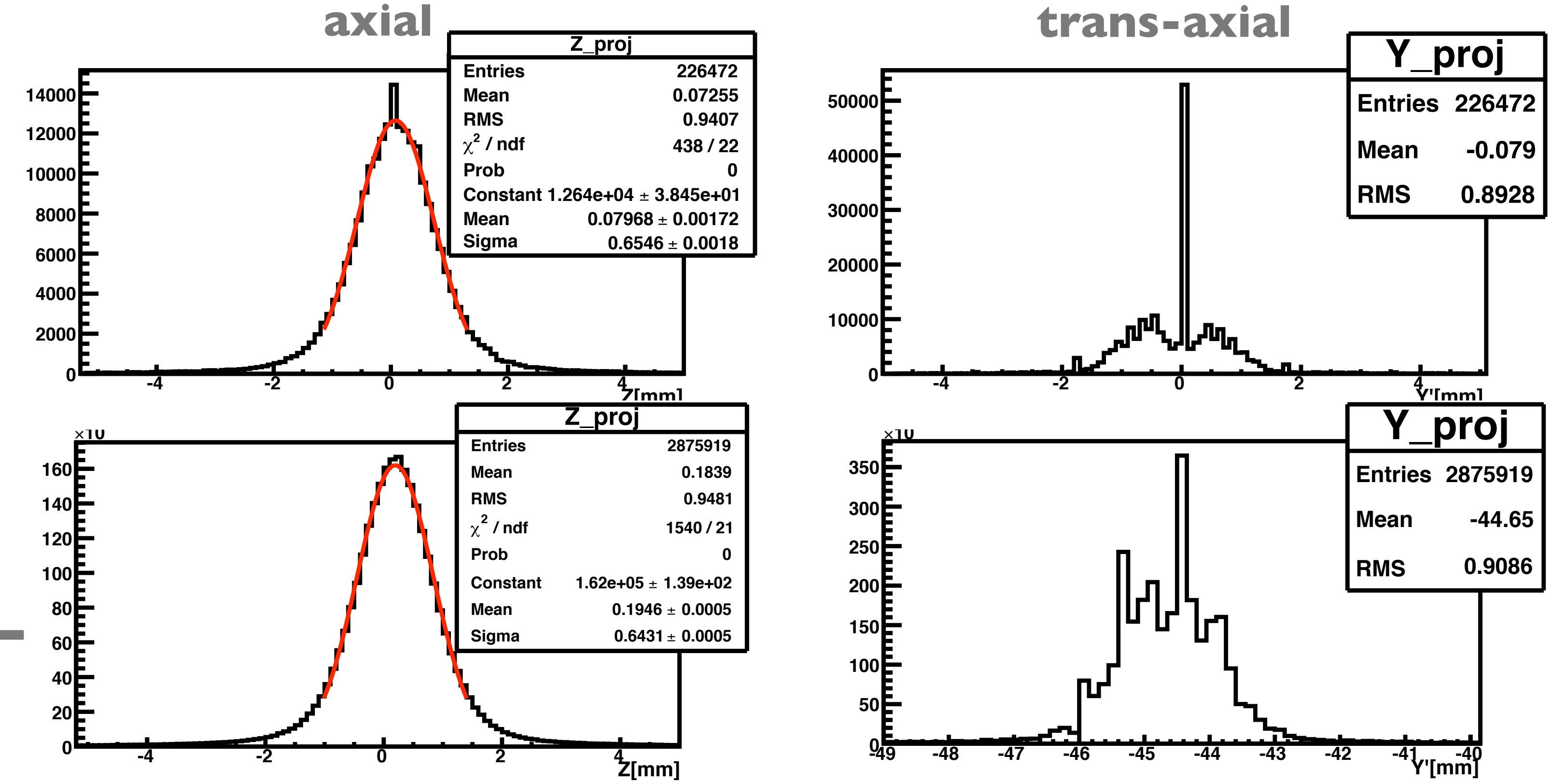


Intersection of LORs with the plane containing the source

axial **trans-axial**

F2F

OBL

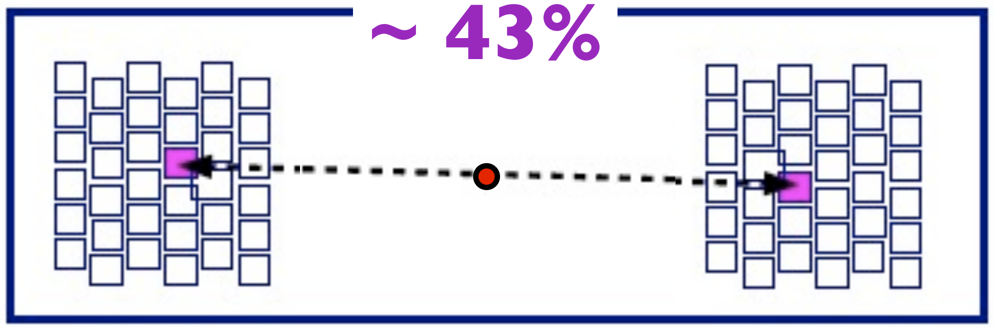


	axial	transaxial
F2F	σ=0.655	RMS=0.893
OBL	σ=0.643	RMS=0.909

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

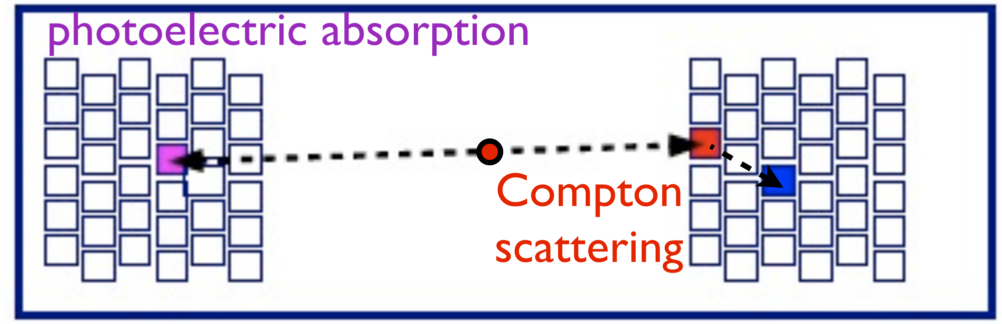
Inter Crystal Scattering (ICS) Events

photoelectric absorption on both modules
"GOLDEN" events



E = 511 keV
E = 511 keV

E_1 < 511 keV
E_2



E = 511 keV
E_1 + E_2 = 511 keV

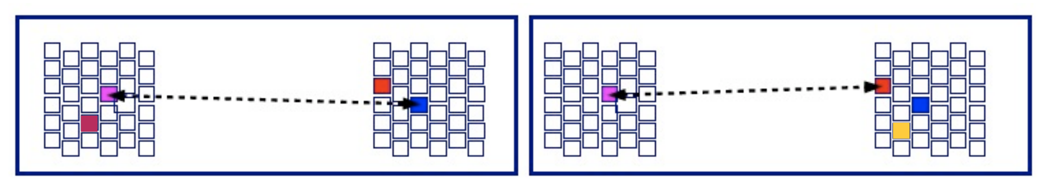
- high granularity in the module
- good energy resolution

=> Possibility to tag inter-crystal scattering events

include them
in the reconstruction
(if correctly identifiable)

enhanced sensitivity

reject them



enhanced resolution

much more important effect with higher fraction of ICS events (larger improvement in the statistics)

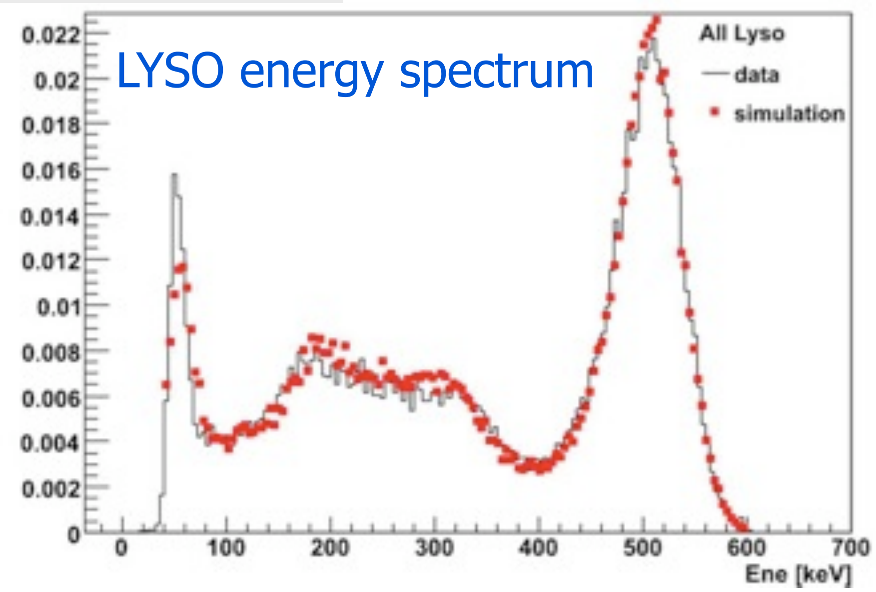
i.e. only slight improvement in the image quality for the AX-PET demonstrator
but significant effect expected in a possible full ring detector

Monte Carlo simulations

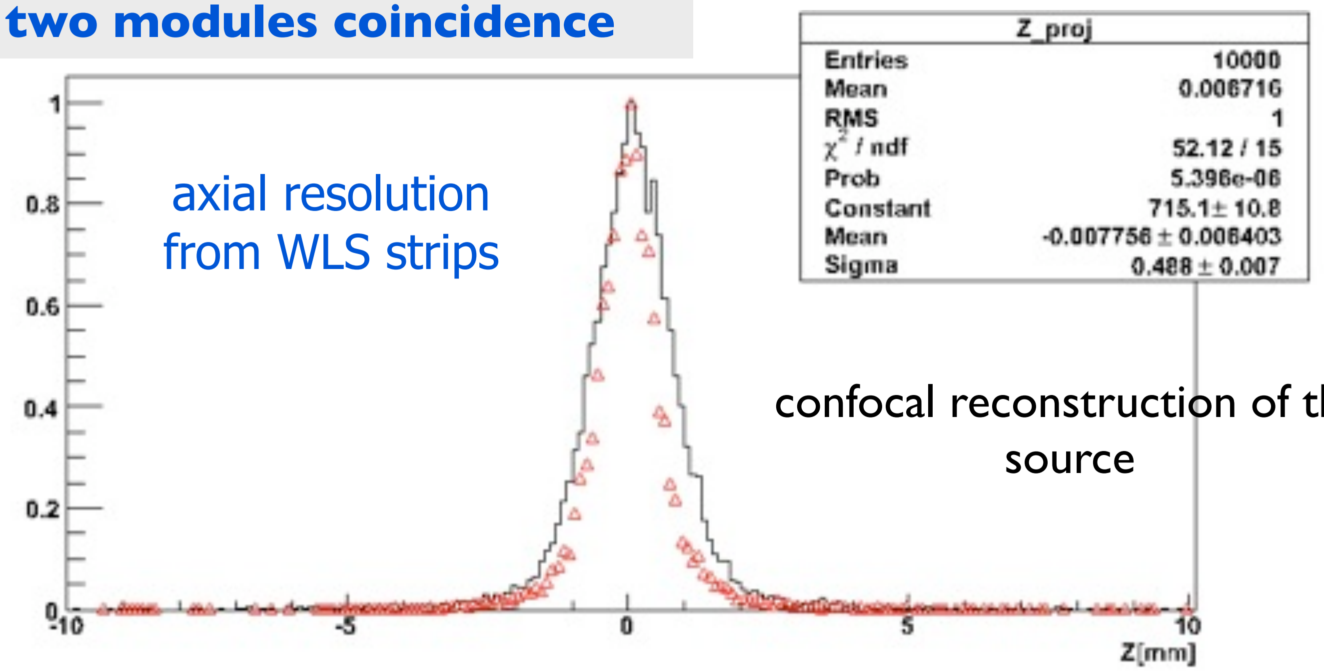
AX-PET : fully simulated device
GATE simulation package

Methods and results :
P. Solevi et al, Phys. Med. Biol. 58 (2013) 5495-5510.

one module only



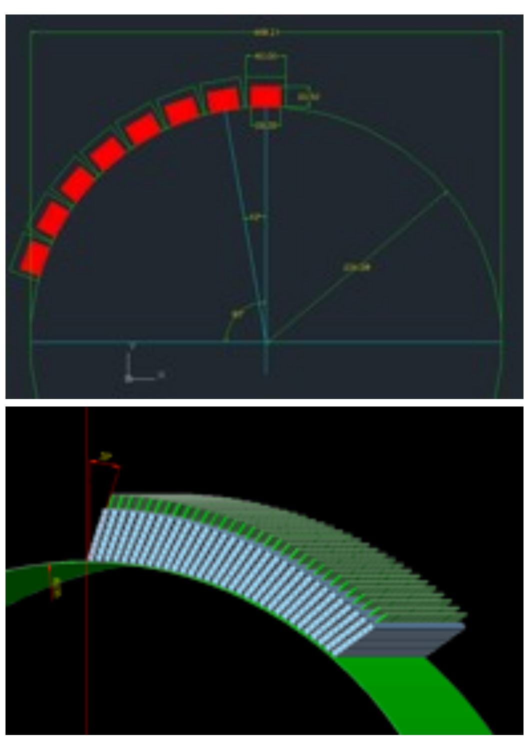
two modules coincidence



confocal reconstruction of the source

<u>Simulation tasks :</u>

for the AX-PET Demonstrator
- better understanding of the detector
- train Compton scattering reconstruction algorithms
- support image reconstruction

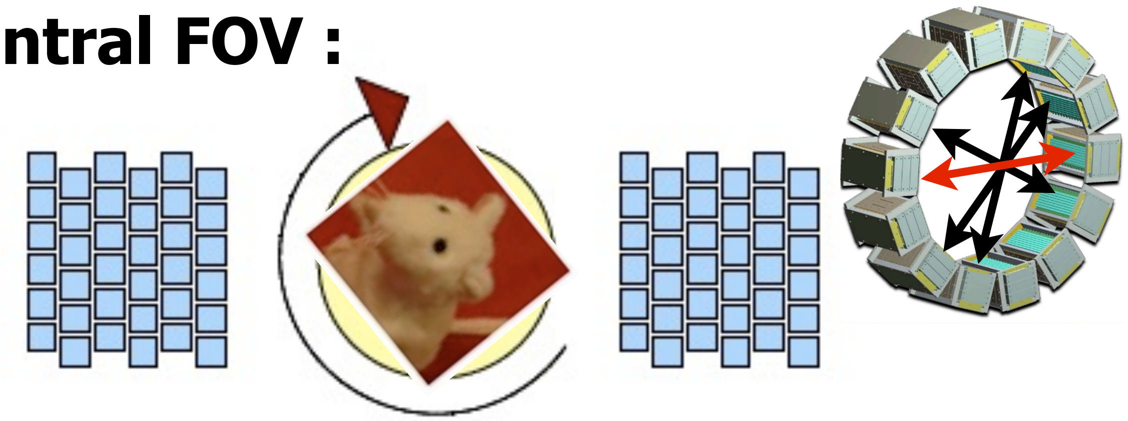


<u>Next : simulate an hypothetical full ring scanner; define its performance</u>

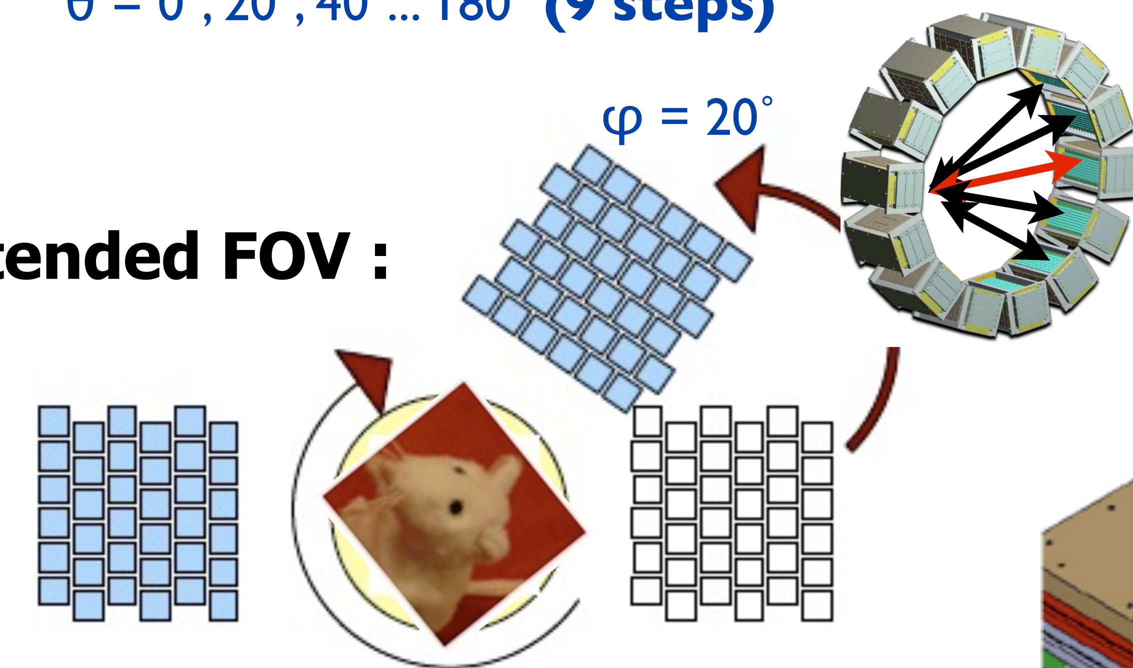
Towards tomographic reconstruction

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

Central FOV :



θ = 0˚, 20˚, 40˚… 180˚ **(9 steps)**

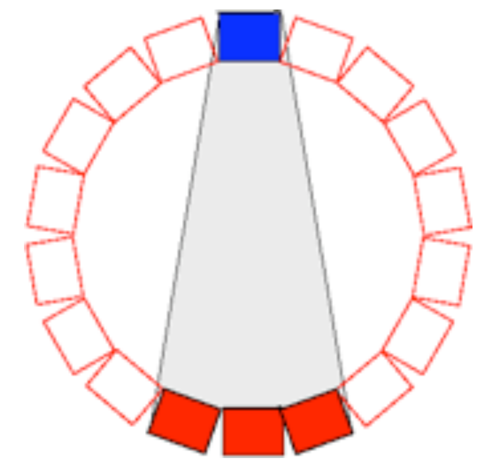


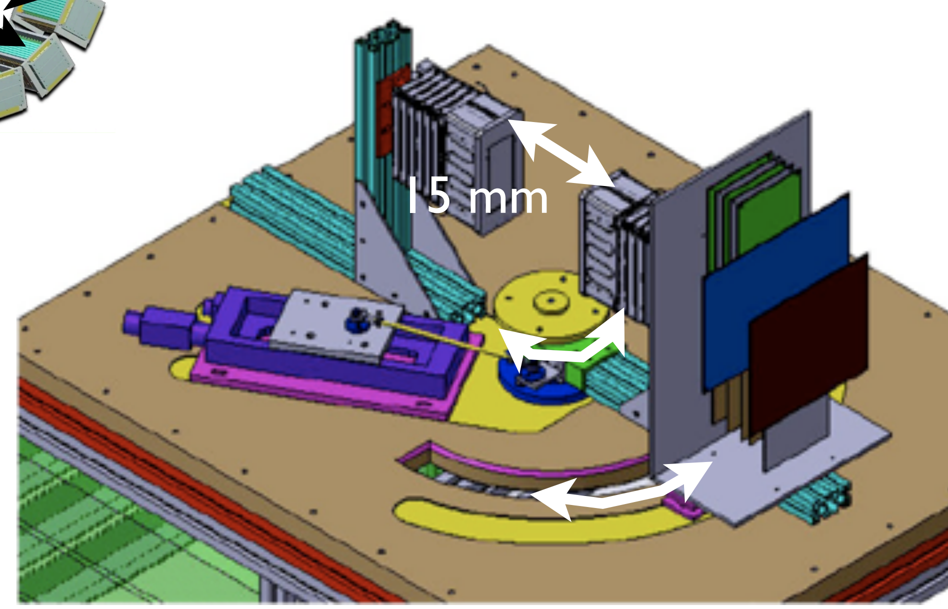
Extended FOV :

θ = 0˚, 20˚, 40˚… 360˚ **(18 steps)**

1 tomographic acquisition
= 27 steps acquisition

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





Reconstruction software :

- dedicated reconstruction software (SOPL, MLEM based) to cope with the many peculiarities of AX-PET

Gillam et al, Phys Med Biol 58 (2013) 2377-2394.

Measurements campaigns

Phantoms 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

Small animals measurement campaign :

@ ETH Zurich (CH), Radio-Pharmaceutical Institute - **Jun 2012**

first animals image reconstruction with an axial PET

ETH, AAA: in-situ cyclotron production of the radiotracer
F-18 based **tracers** (F-18 in water solution or FDG)
- **$t_{1/2}$ ~ 110 mins**
- Concentration diluted in water; **A_0: few MBq up to ~ 100 MBq**

NEMA phantom

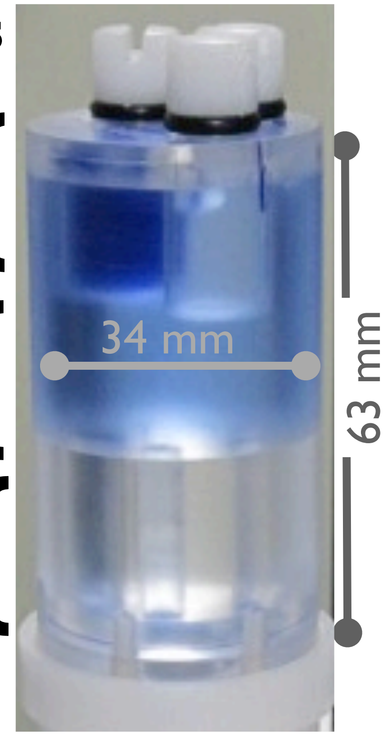
NEMA-NU4 IQ (mouse) phantom :

Three regions in the same phantom to address three different aspects

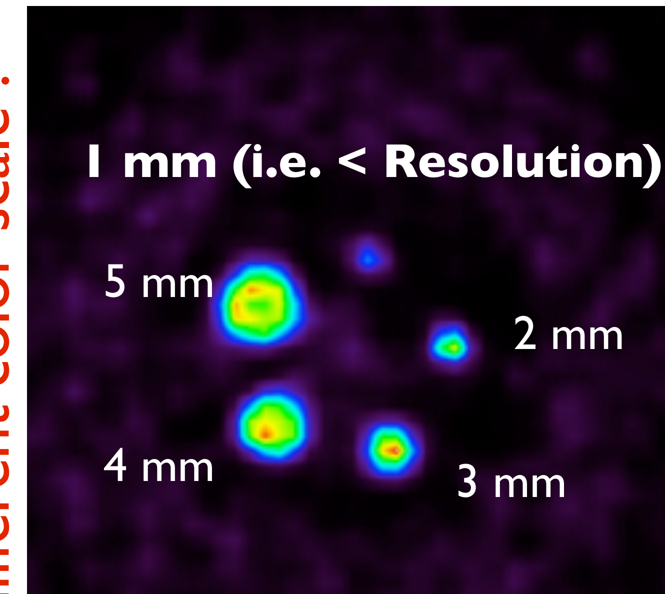
Hot & Cold rods for **contrast**

Homogeneous cylinder for assessing the **ability to reconstruct homogeneous distributions**

Series of small rods for **resolution**



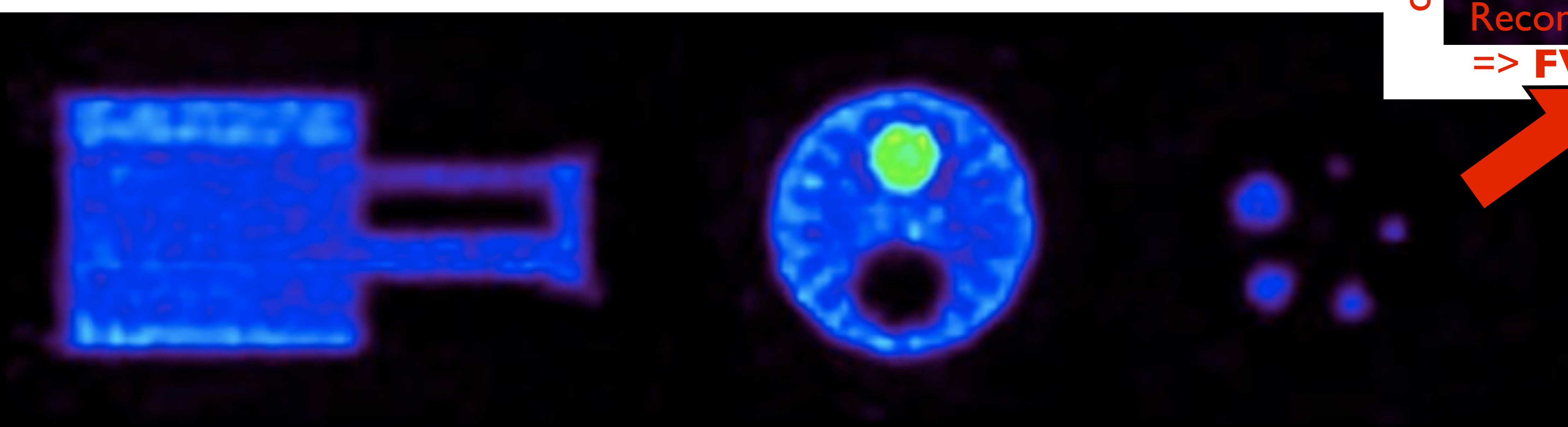
different color scale !



Reconstructed 1 mm rod

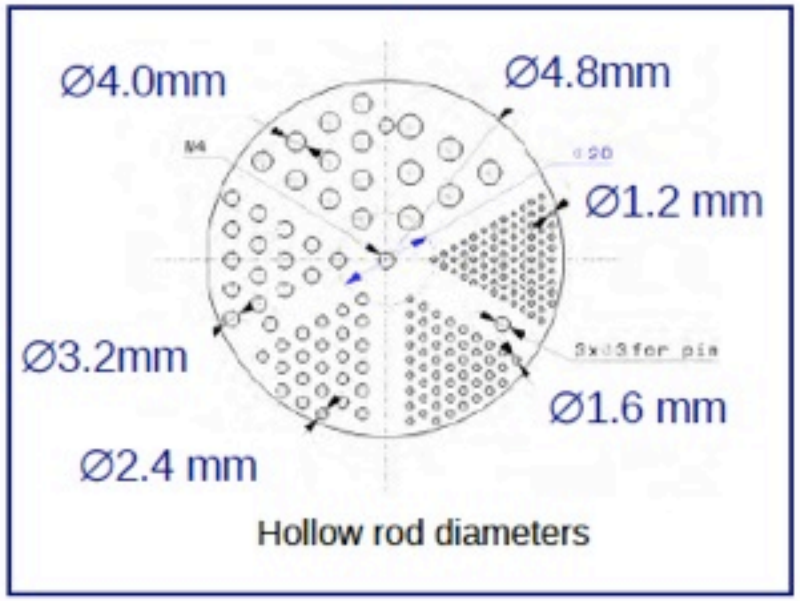
=> **FWHM ~ 1.6 mm**

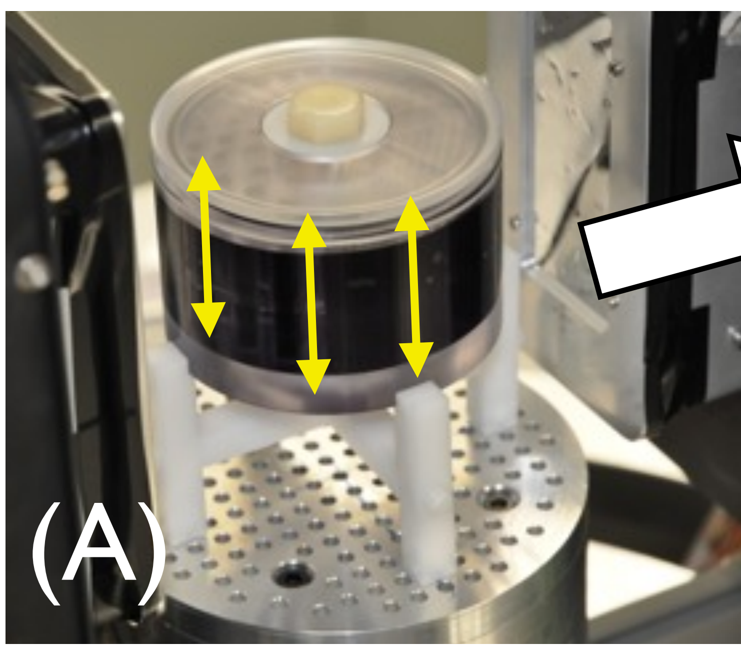
NEMA phantom hot / cold / warm - AAA



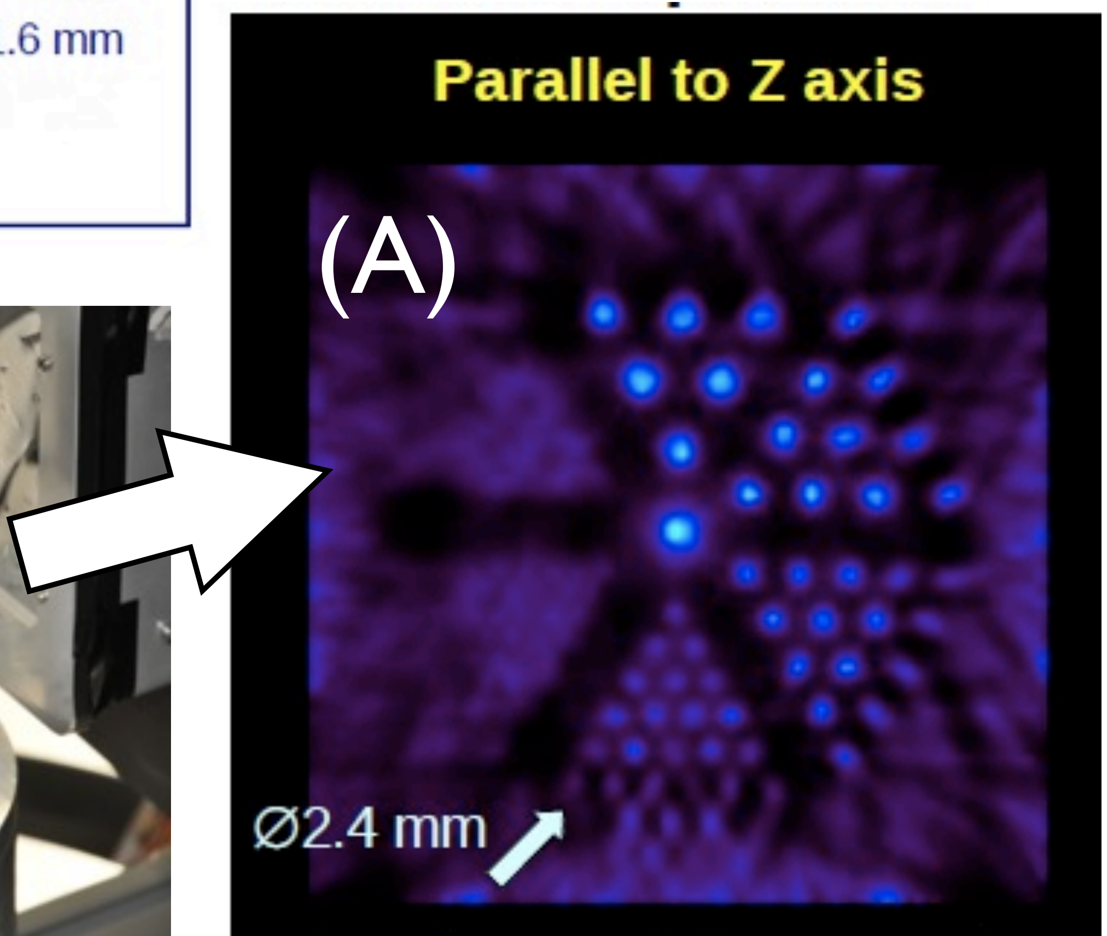
Resolution phantom

Mini Deluxe phantom





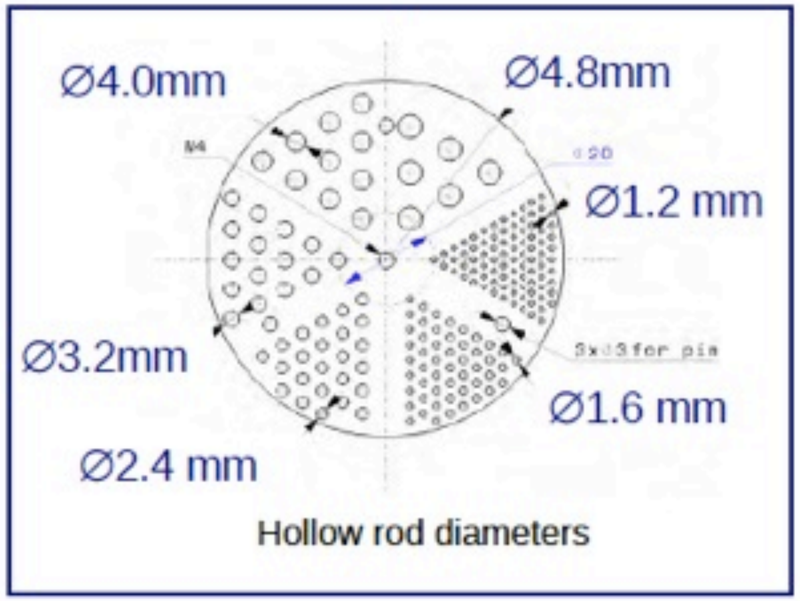
Rods oriented parallel to Z axis

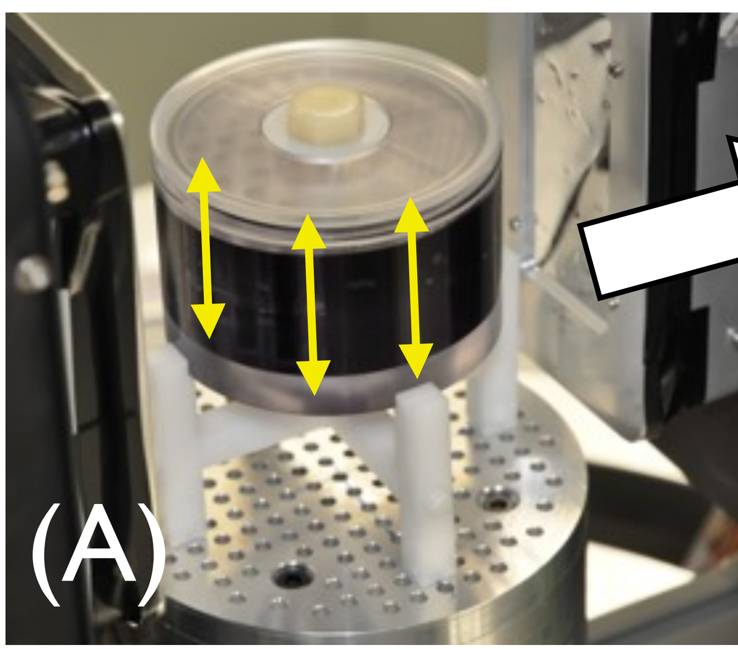


- Fixed time acquisition: 120 s /step
- 60 iterations + post-reconstruction smoothing
- No corrections
- Artefacts due to data truncation (FOV too small...)

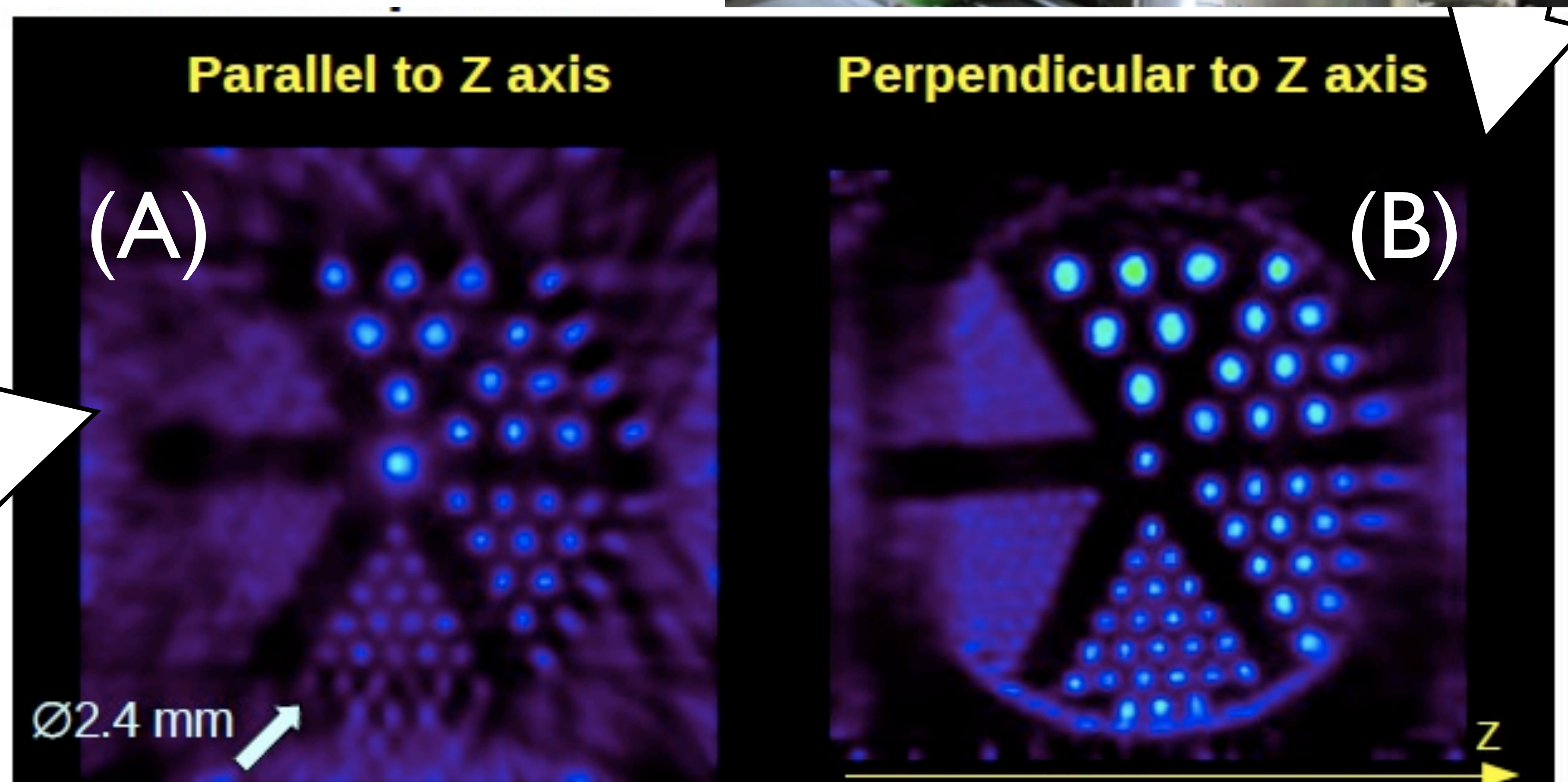
Resolution phant

Mini Deluxe phantom





Rods oriented parallel to Z axis

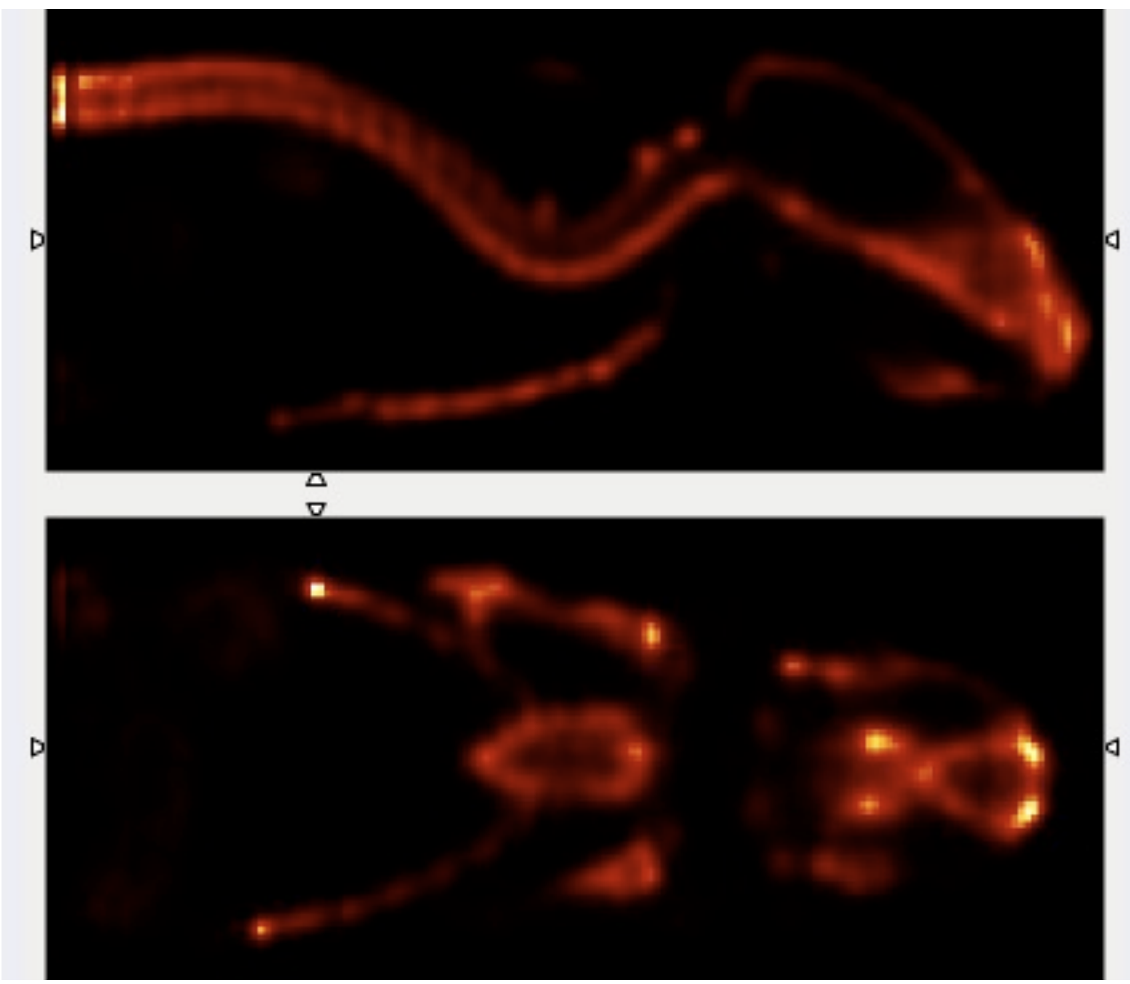


- Fixed time acquisition: 120 s /step
- 60 iterations + post-reconstruction smoothing
- No corrections
- Artefacts due to data truncation (FOV too small...)

Small animal reconstructed images

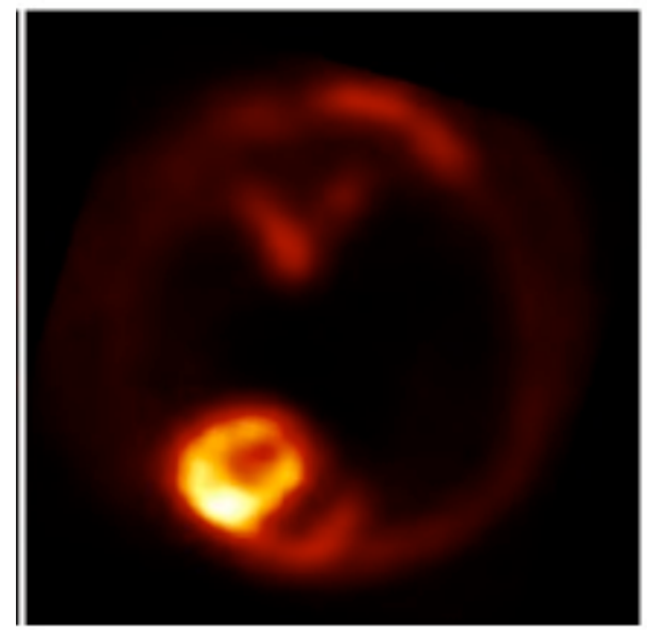
- **SMALL ANIMAL IMAGING CAMPAIGN**
  - **F-18 bone scan** of one young rat (post-mortem)
  - two **FDG studies**, one young rat, one mouse (post-mortem)
  - at Animal Imaging Center - PET @ ETH Zurich, June 2012

Rat F-18 => Bone scan



- **fine structure visible (high spatial resolution)**
- **large axial coverage (single step acquisition)**

Rat FDG => zoomed coronal image of the rat hearth



low contrast regions (ventricular myocardium) visible

first rodent images from a PET with axial geometry !

satisfactory quality of the reconstructed images – despite the limitations of the experimental setup (i.e. two modules only, large crystals cross section)

Small animal reconstructed images

AX-PET Demonstrator successfully demonstrated the potential of axially oriented crystals in a PET

AX-PET Collaboration

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Università e Sezione INFN di Cagliari, Italy.

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- experiment at CERN, Geneva
- background of the collaboration : high energy physics and medical imaging (Valencia, IFIC)

AX-PET Collaboration

- experimen
- backgroun

AX-PET Collaboration

AX-PET

- experimen
- backgroun

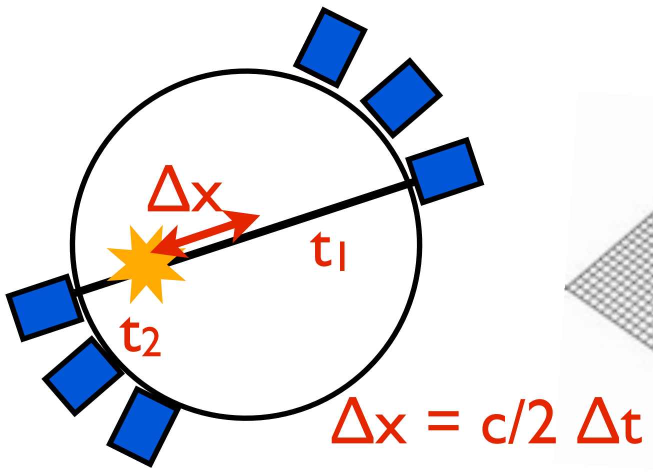
Beyond AX-PET ...

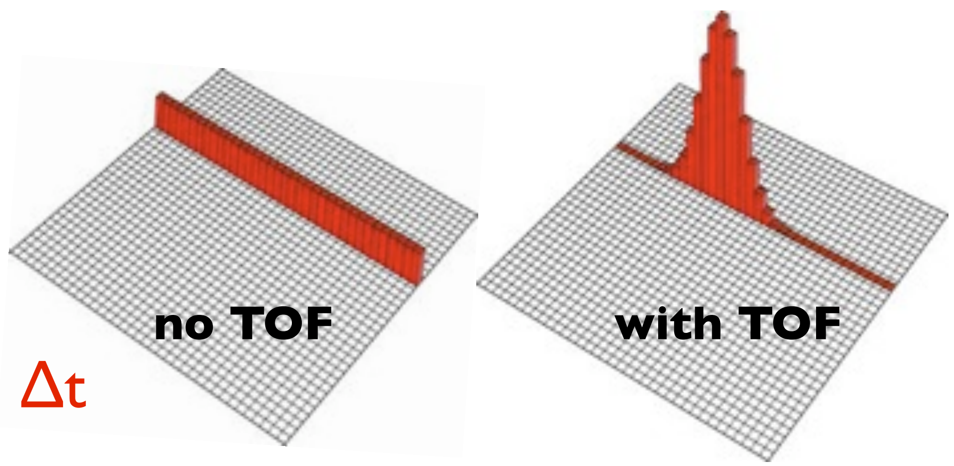
Studies on 100 mm long LYSO crystals [with single crystals setups, not full demonstrator]
- timing properties
- dual sided readout => axial resolution without WLS strips

Current trends in PET instrumentation

1. Towards TOF-PET

measure the time difference in the arrival of the two photons to constraint the position of the interaction point along the line of response i.e. improve S/N



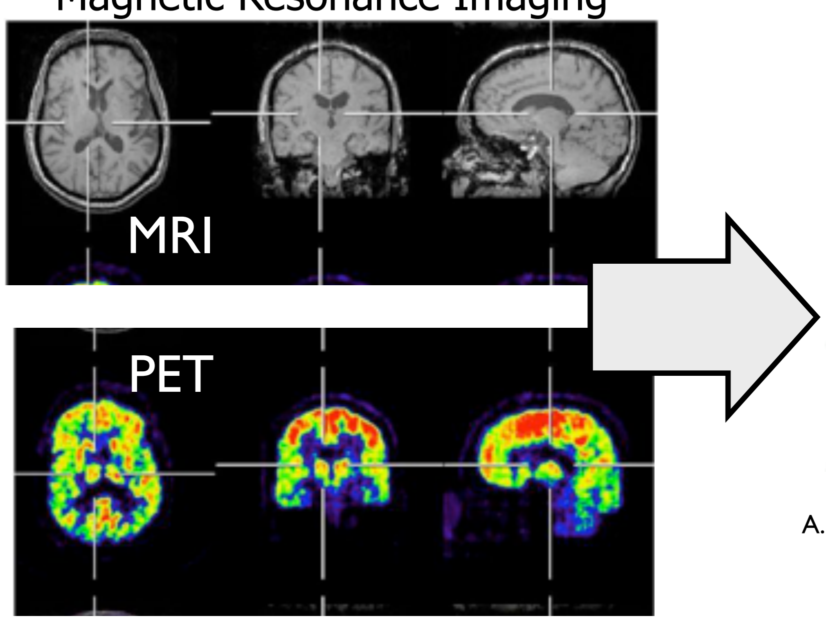


Δ t	Δ x
500 ps	7.5 cm
100 ps	1.5 cm

2. Towards PET-MRI

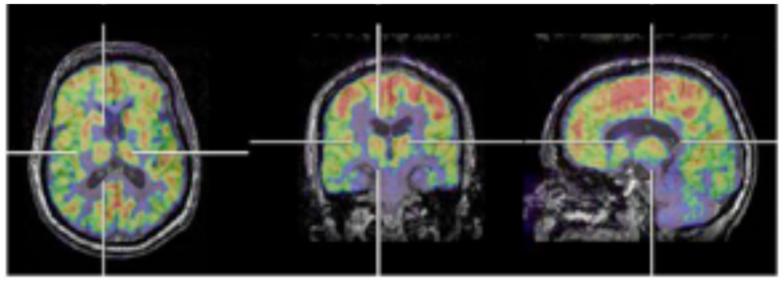
combine two different and complementary imaging technique to best exploit the potential of nuclear imaging

Magnetic Resonance Imaging



Positron Emission Tomography

Combined PET - MRI



A.Del Guerra, CERN Academic Training 2009

morphological information from MRI [**excellent resolution**]

+

functional information from PET [**excellent sensitivity**]

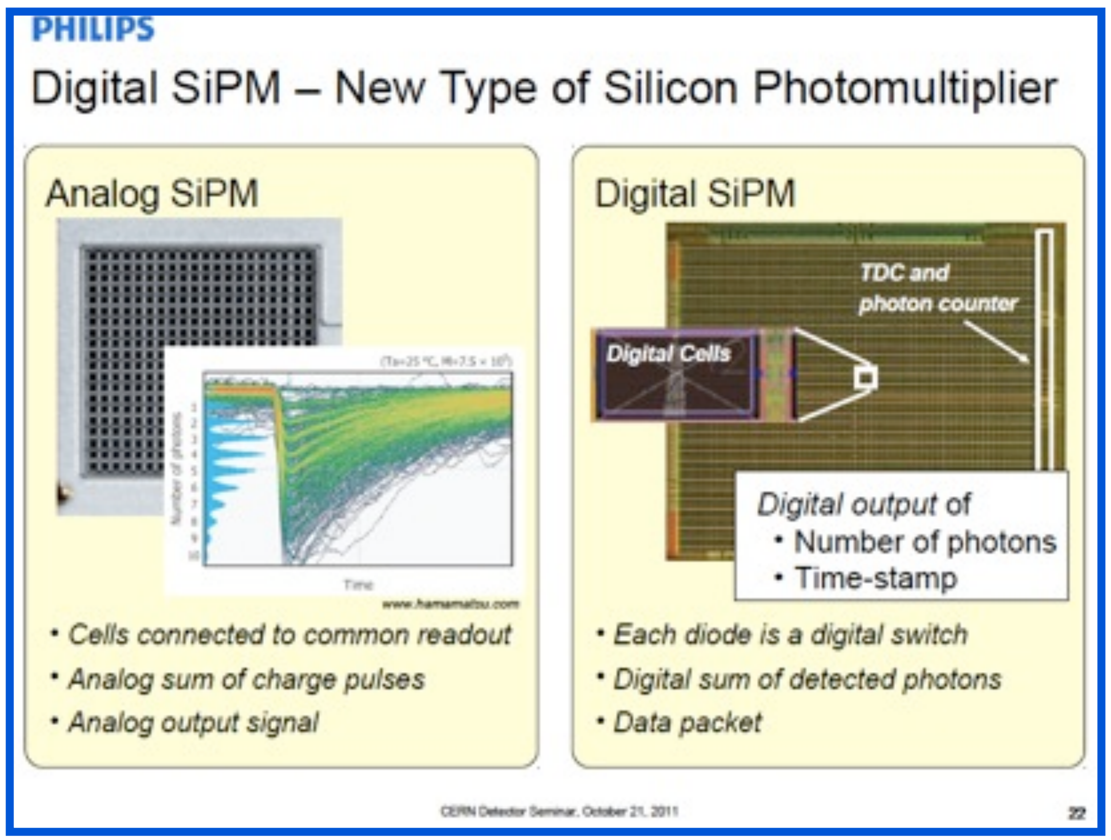
AX-TOF-PET : would that be possible?

Is it possible to add TOF capabilities to an AX-PET like detector?
Timing information required, with **excellent timing resolutions**

Philips digital SiPM (dSiPM)

- fully digital implementation of SiPM
- high resolution TDC (19.5 ps resolution) => time information ; ~ 50 ps intrinsic time resolution
- high compactness, high level of integration

Thomas Frach, CERN Detector seminar, Oct 2011

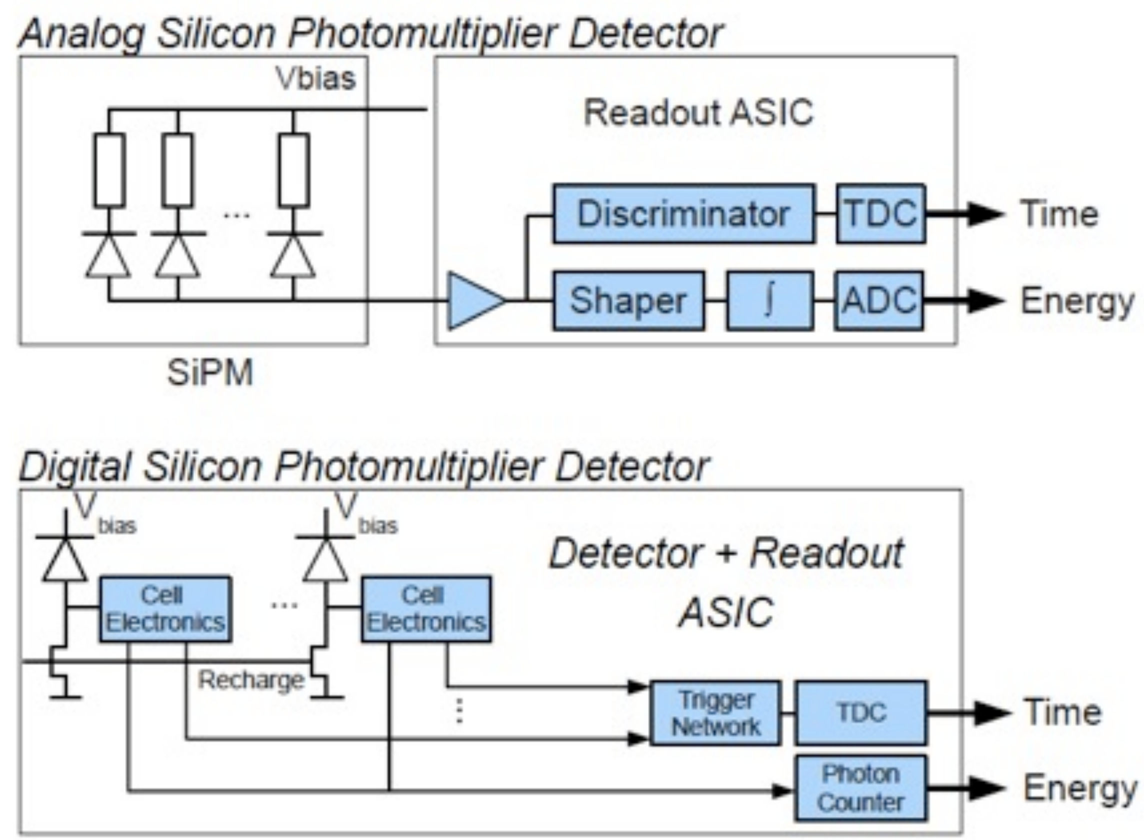

PHILIPS

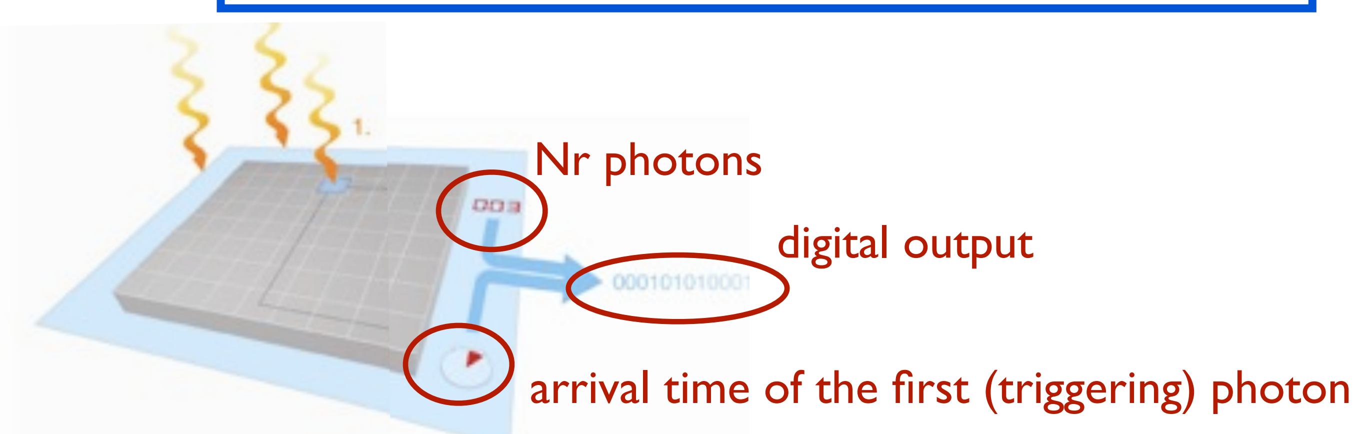
Digital SiPM – New Type of Silicon Photomultiplier

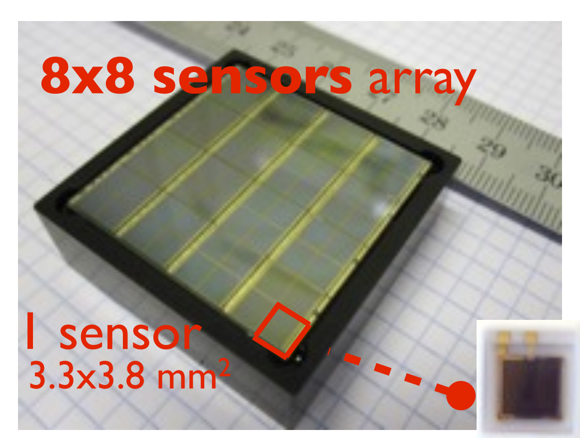
Analog SiPM
- *Cells connected to common readout*
- *Analog sum of charge pulses*
- *Analog output signal*

Digital SiPM
- *Each diode is a digital switch*
- *Digital sum of detected photons*
- *Data packet*

CERN Detector Seminar, October 21, 2011 22



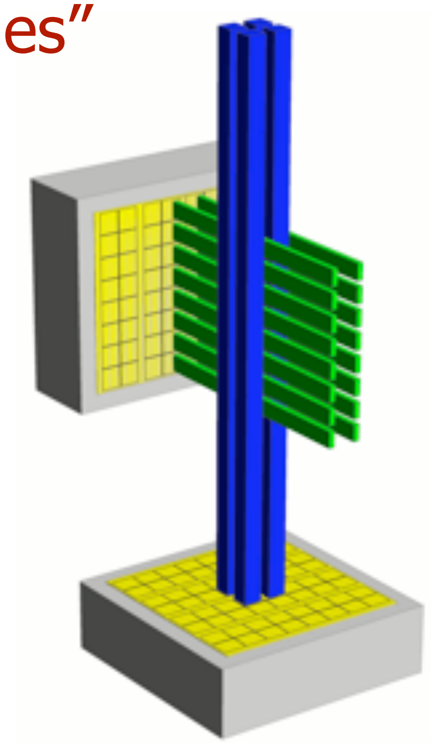


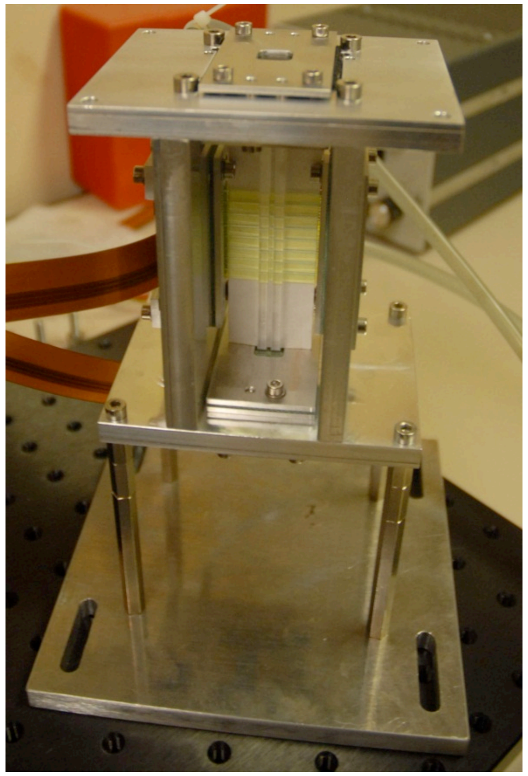


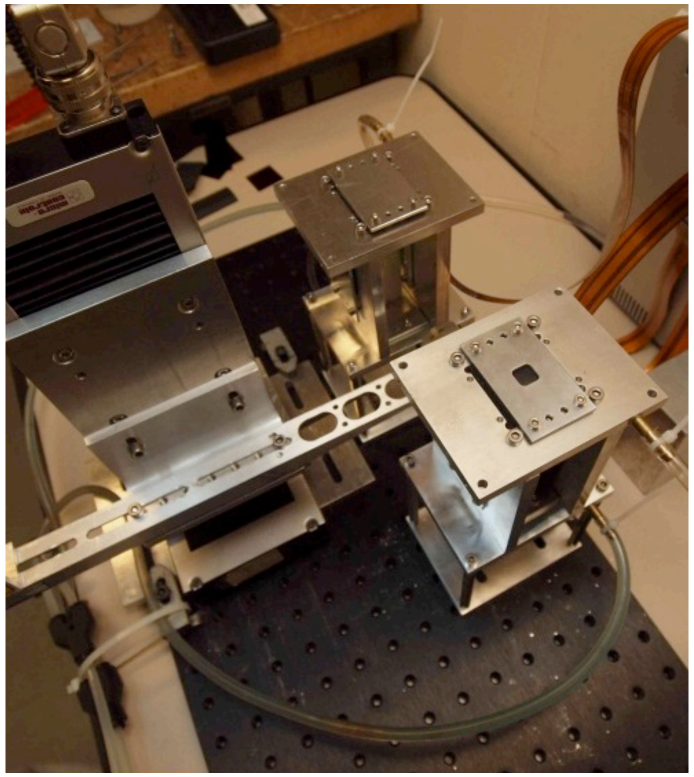
dSiPM as alternative photodetectors for AX-PET

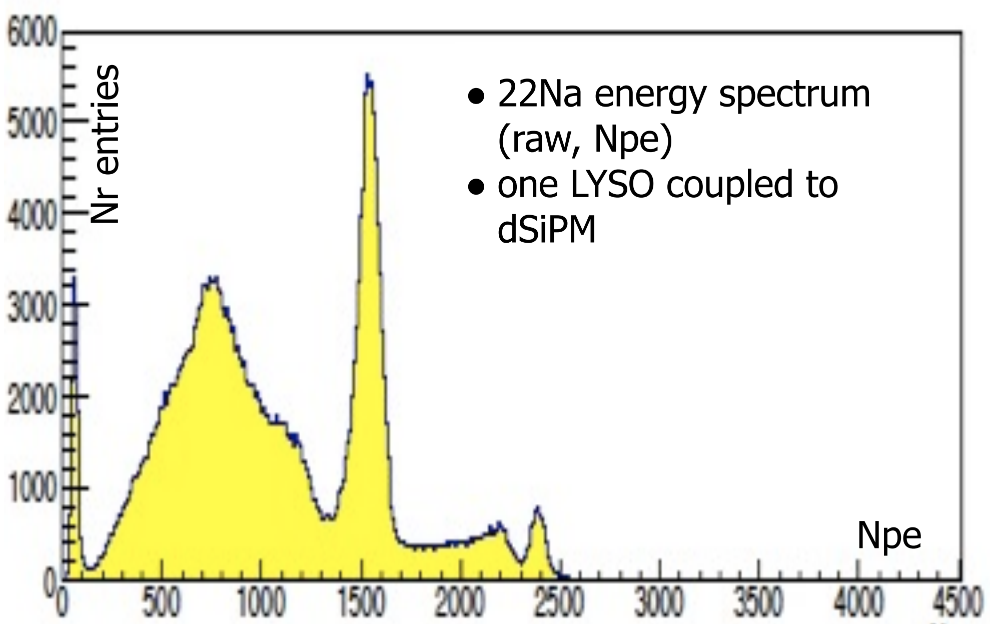
"digital (small-scale) AX-PET modules"

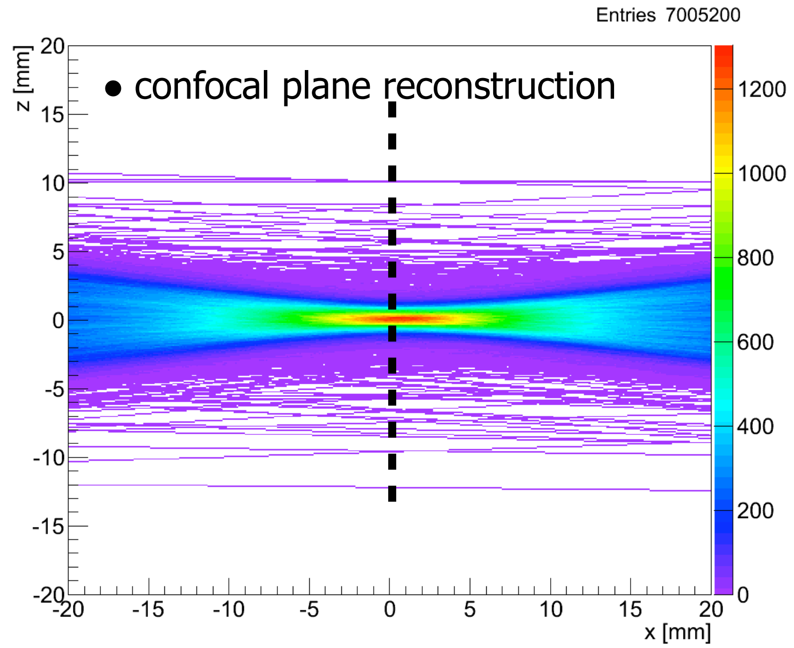
- **two modules**
- **identical detector elements as AX-PET**
- reduced Nr channels
- 2 Layers; 2 LYSO and 8 WLS / layer
- **coupled to dSiPM**
- 22Na source characterization measurements (individually and in coincidence)











Results of the characterization measurements:

- **Light yield : ~ 1500 pe** (at 511 keV)
- **ΔE/E ~ 14%** @511 keV (after en.calibr.)
- **R_z ~ 1.22 mm**, FWHM (**in coincidence**)
- **$R_{z, mod}$ ~ 1.71 mm**, FWHM

The usage of dSiPM does not compromise the performance already achieved by the AX-PET detector

ADDITIONAL HIGH RESOLUTION TIMING INFORMATION

Coincidence timing resolution (CRT)

Fully exploit dSiPM timing capabilities => CRT ?

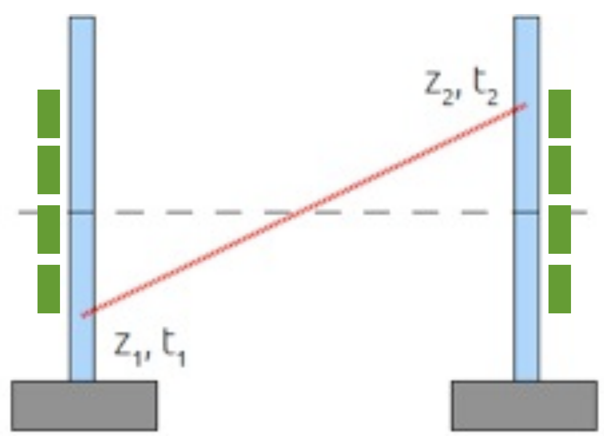
100 mm long crystals =>arrival time at photodetector depends on the axial coordinate

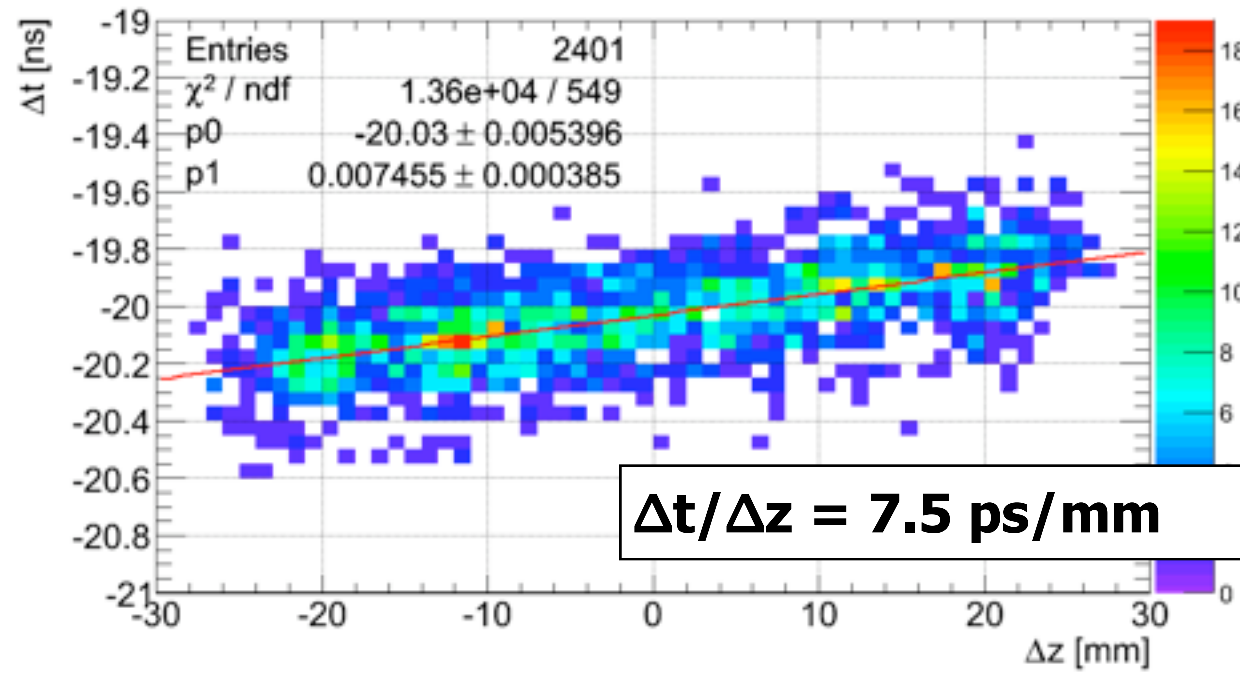
Coincidence timing resolution (CRT)

Fully exploit dSiPM timing capabilities => CRT ?

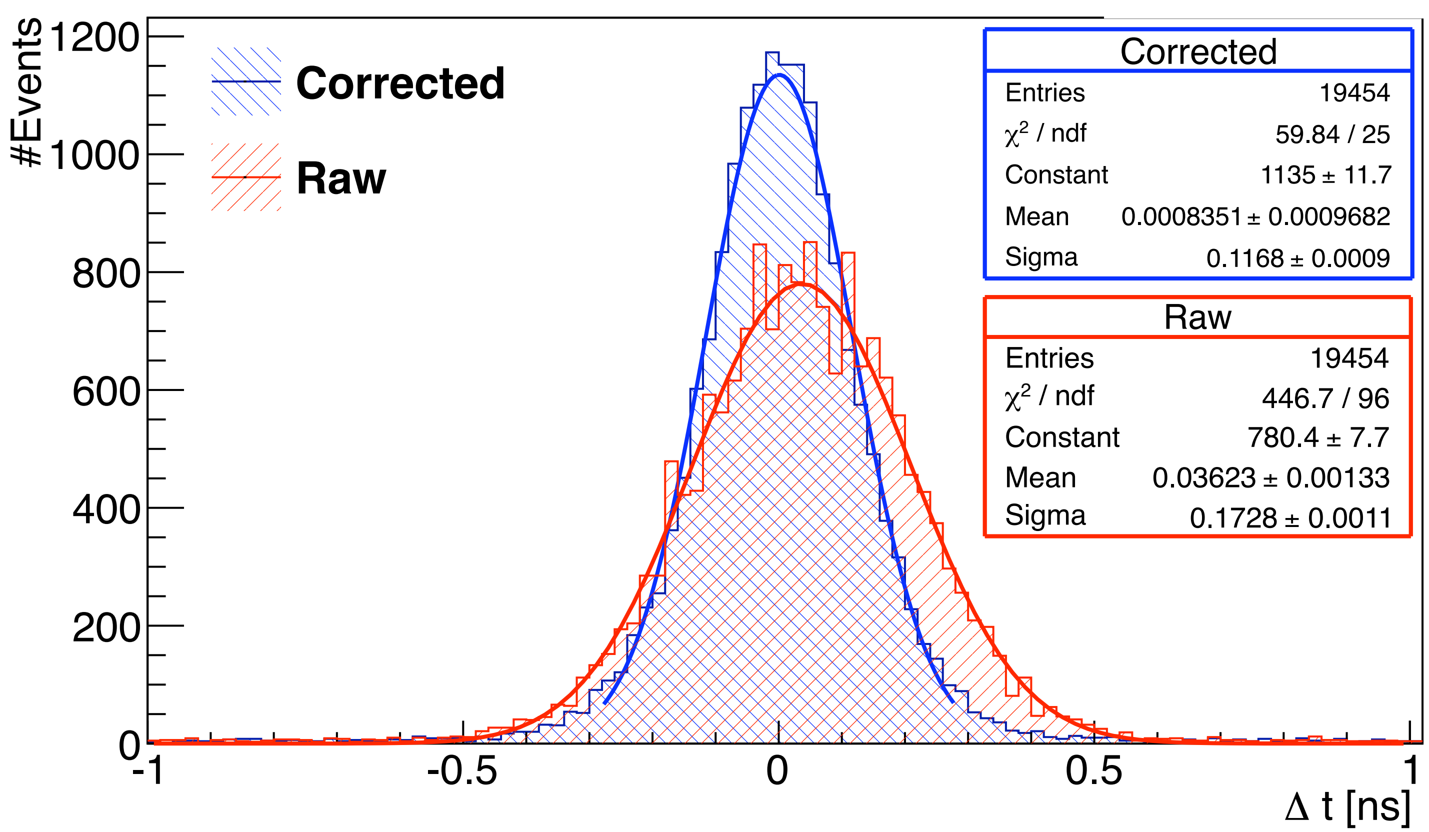
100 mm long crystals =>arrival time at photodetector depends on the axial coordinate

(a) correct for the axial coordinate
(using information from WLS)





Δt/Δz = 7.5 ps/mm



not corrected for axial coord.

CRT ~ 406 ps FWHM

module t_res ~ 287 ps FWHM

corrected for axial coord.

CRT ~ 269 ps FWHM

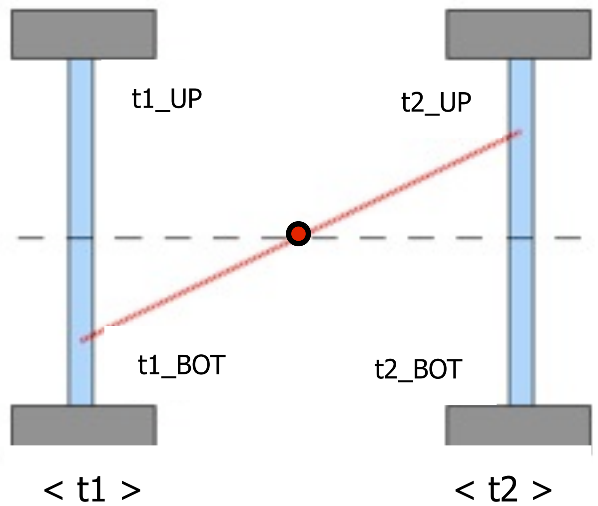
module t_res ~ 190 ps FWHM

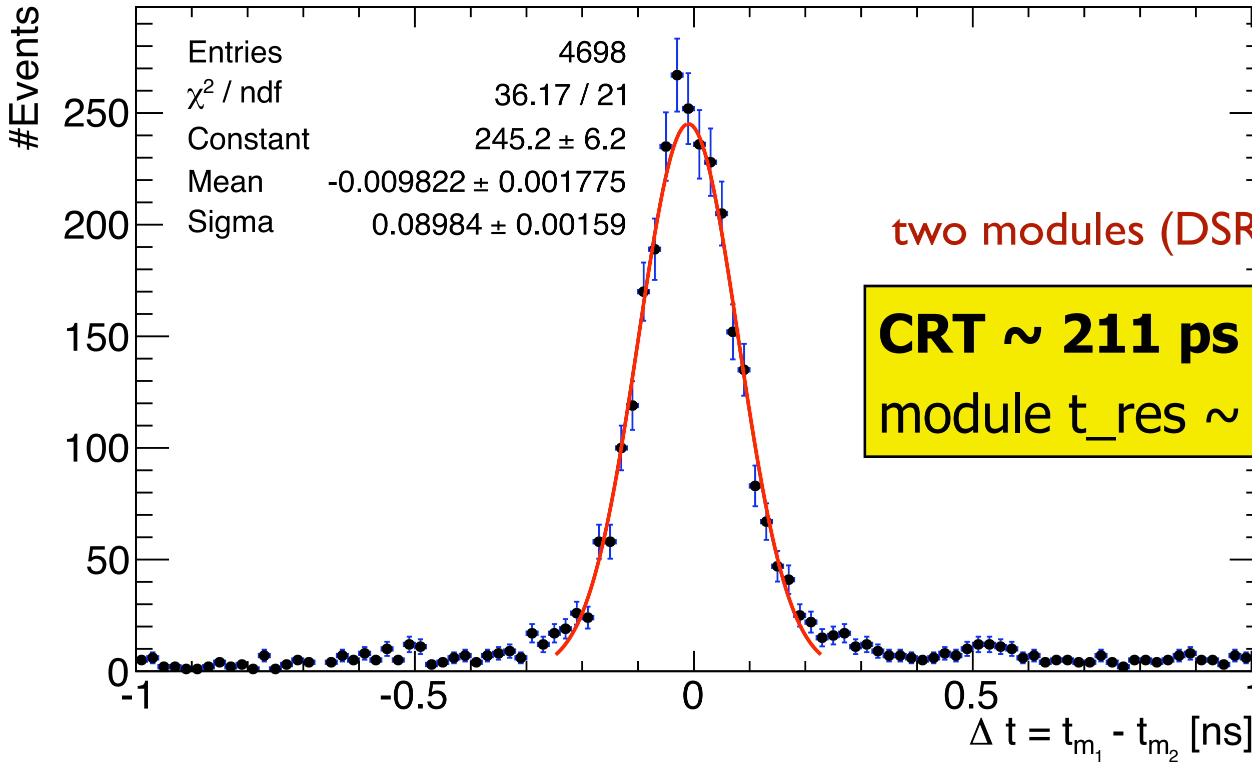
Coincidence timing resolution (CRT)

Fully exploit dSiPM timing capabilities => CRT ?

100 mm long crystals =>arrival time at photodetector depends on the axial coordinate

(b) use dual sided readout
average time information

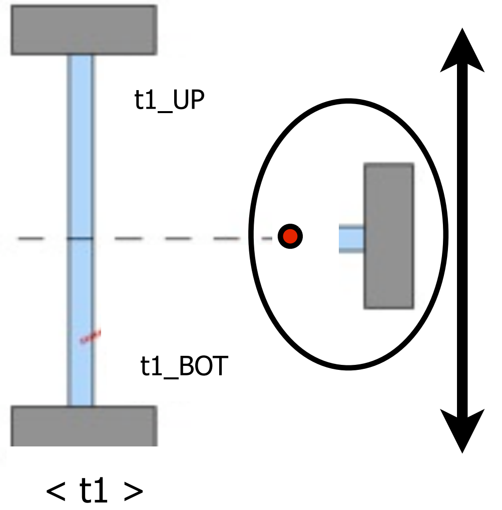


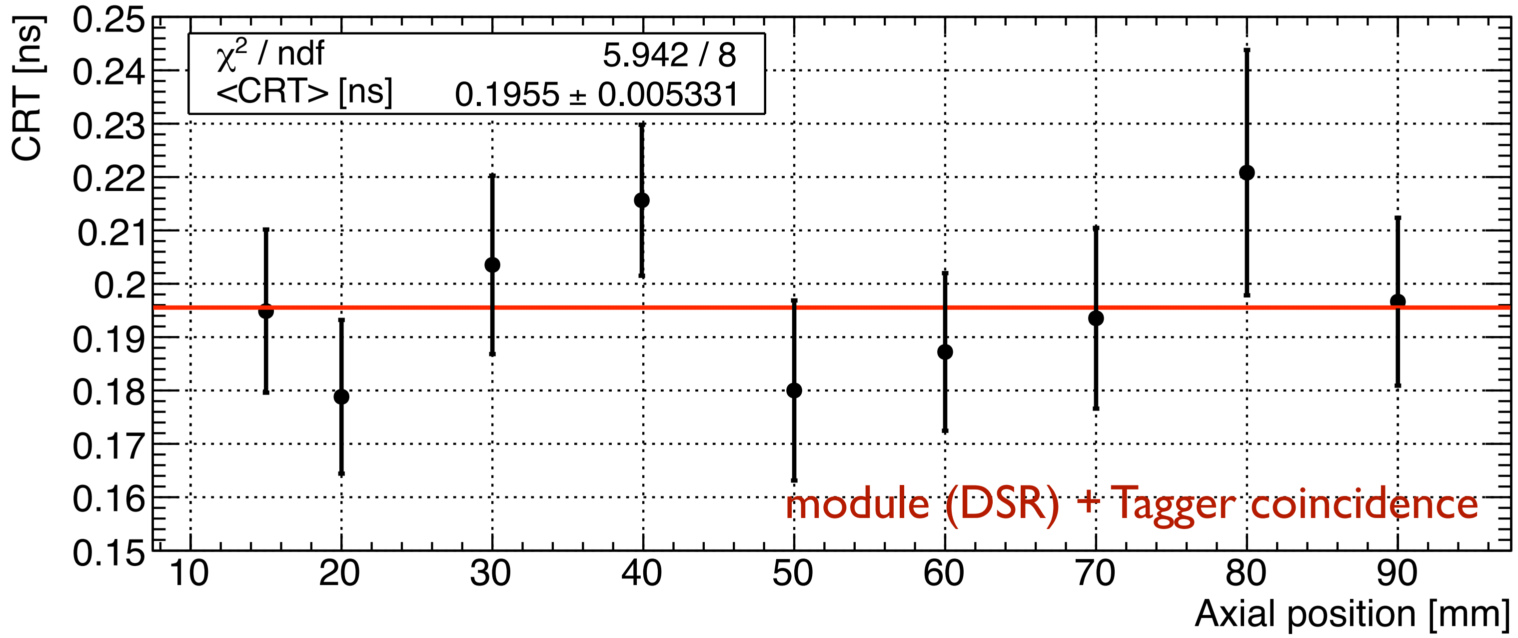


two modules (DSR) coincidence

CRT ~ 211 ps FWHM
module t_res ~ 149 ps FWHM

AXIAL scan





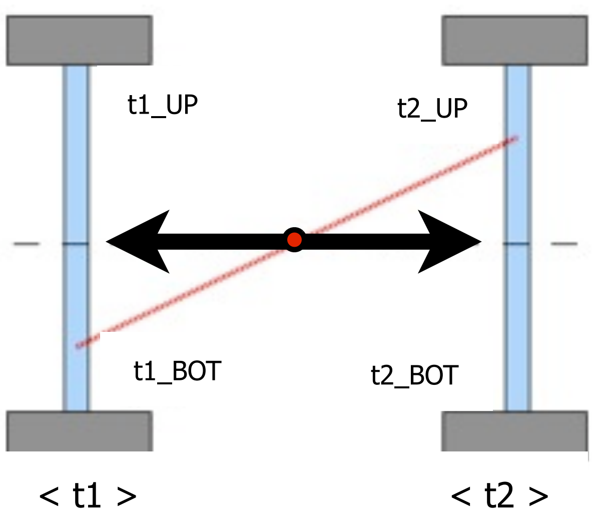
independent on axial coordinate

Coincidence timing resolution (CRT)

Fully exploit dSiPM timing capabilities => CRT ?

100 mm long crystals =>arrival time at photodetector depends on the axial coordinate

(b) use dual sided readout
average time information



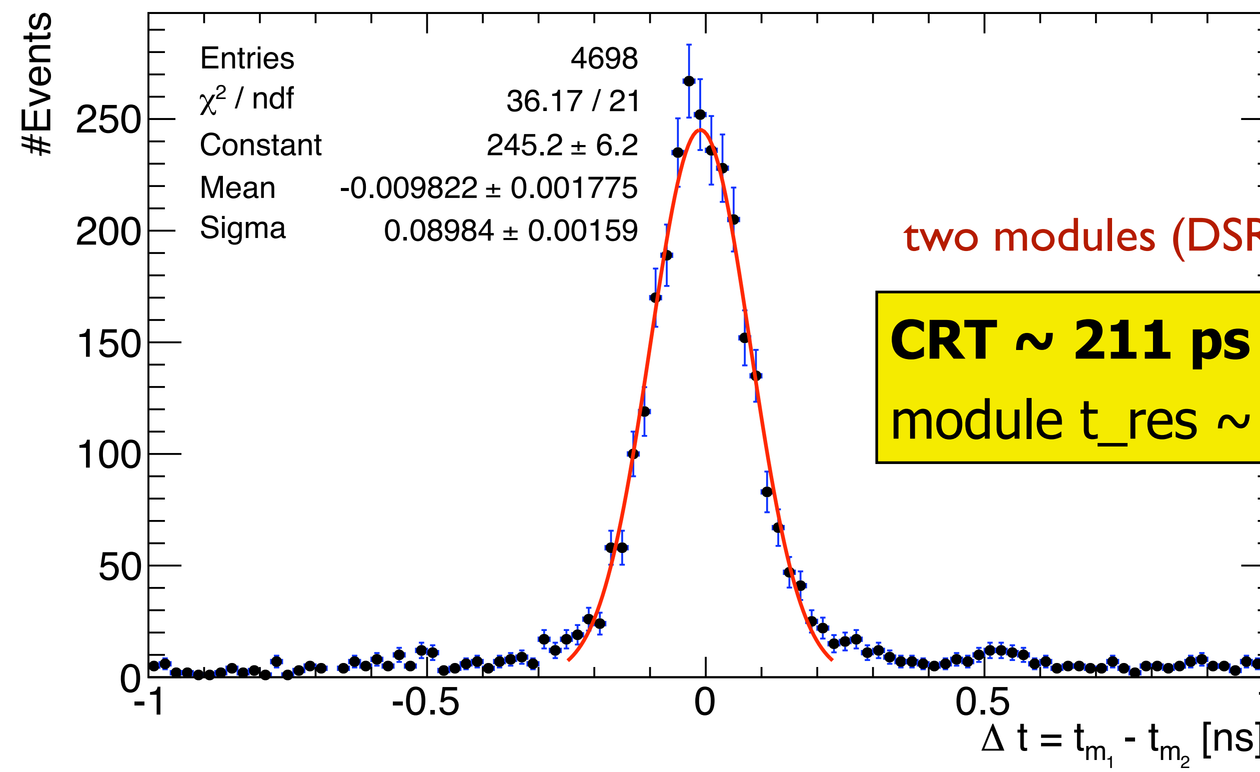
horizontal scan

independent on the horizontal position along the FOV

Excellent timing resolutions achieved, constant inside the entire field of view.

There is a TOF potential for an AX-PET like detector

10.1016/j.nima.2013.10.049 (in press)



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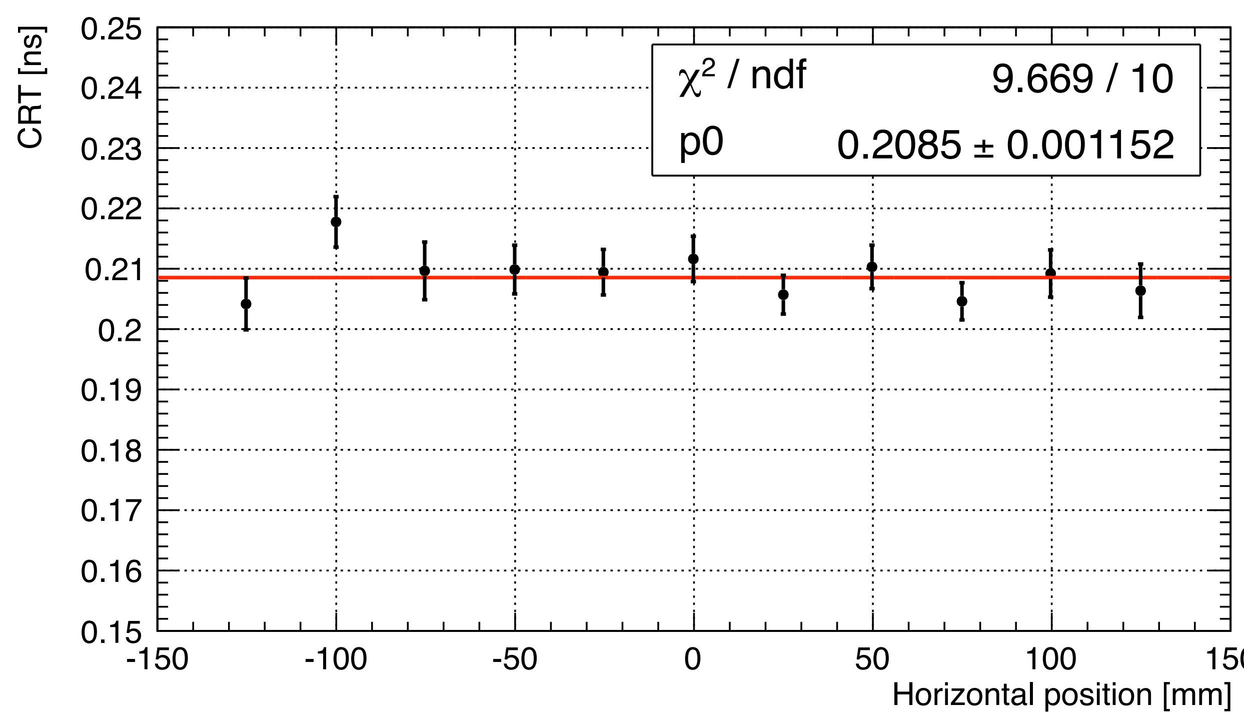
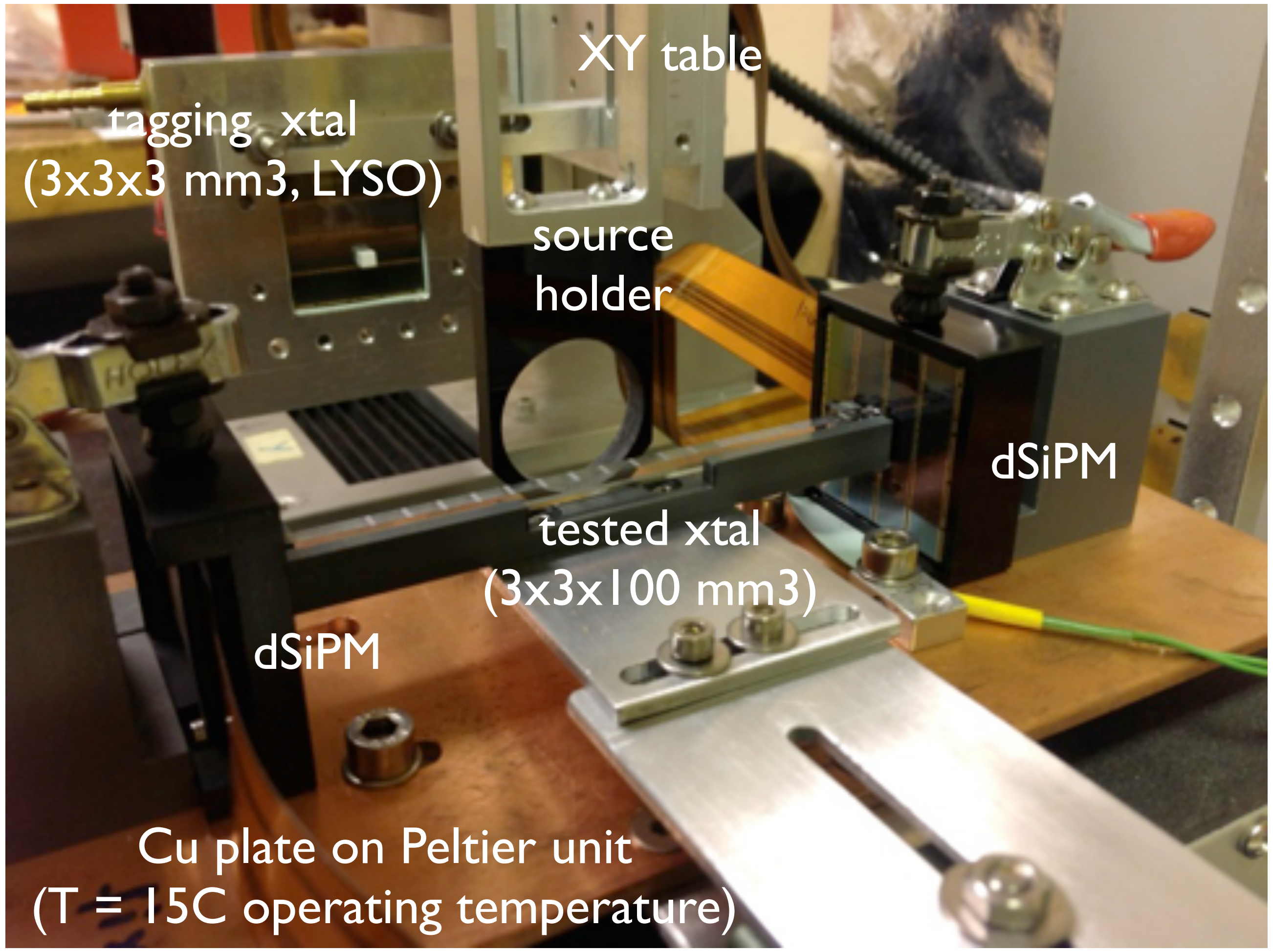
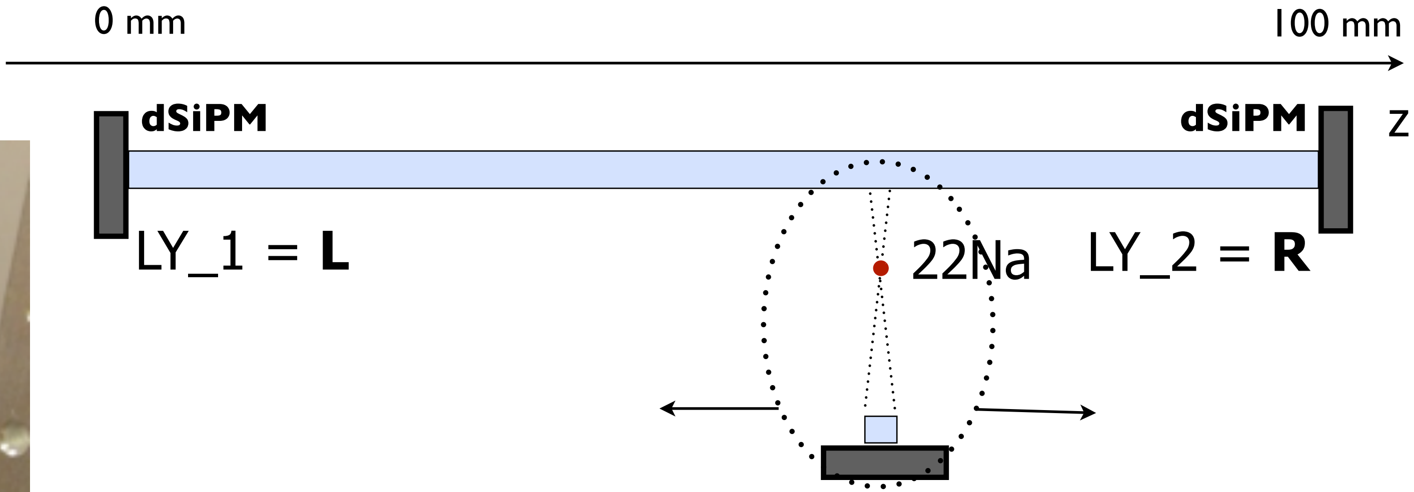


Axial coordinate of long dual sided readout crystal

Are there alternative ways to **define the axial coordinate <u>without WLS strips</u>** ?
Which **axial resolution** can be achieved?

- dual sided readout crystals
- timing difference technique ? not possible, because of too high required time resolution
- light sharing techniques => **(R-L)/(R+L)**





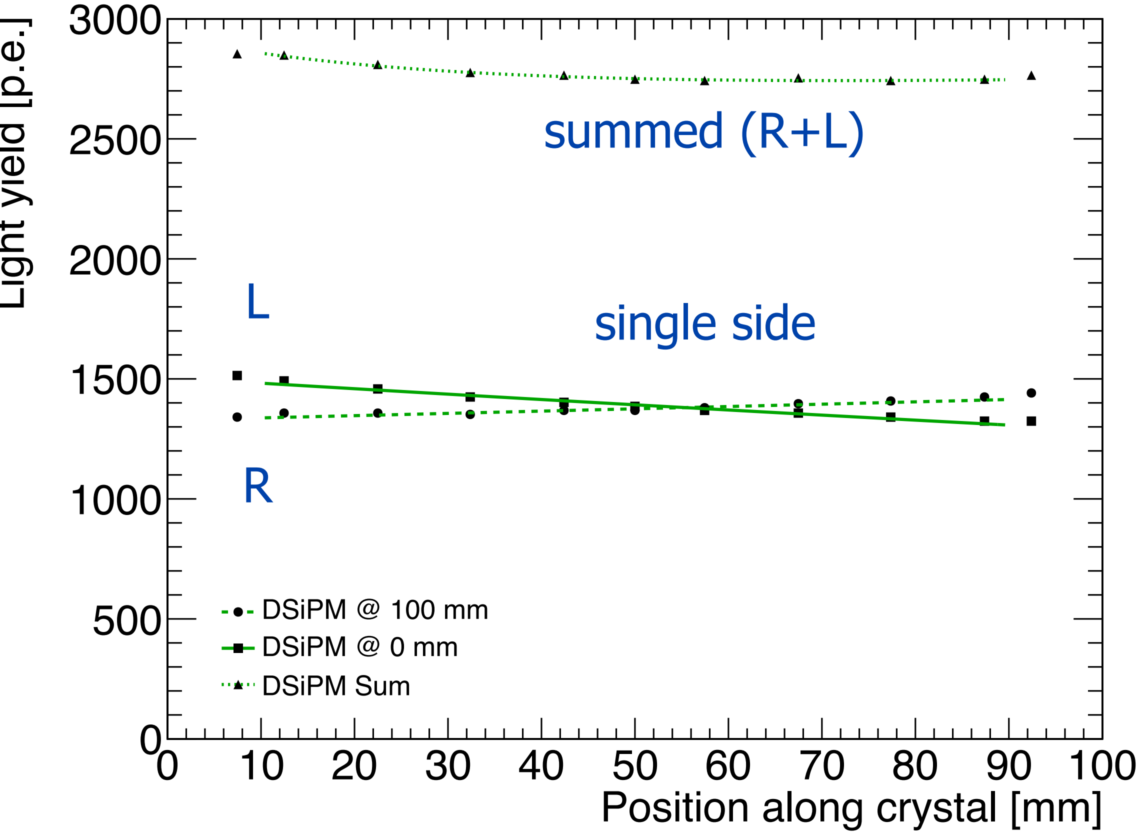
22Na source + tagging crystals at different axial positions

- original idea of the axial PET (HPD-PET)
  J.Seguinot et al, "Il Nuovo Cimento" C29(04), 2006
- also inspired by recent work from University of Manitoba (group A. Goertzen)
  F. ur-Rehman et al, 2011 IEEE. doi:10.1109/NSSMIC.2011.6153681

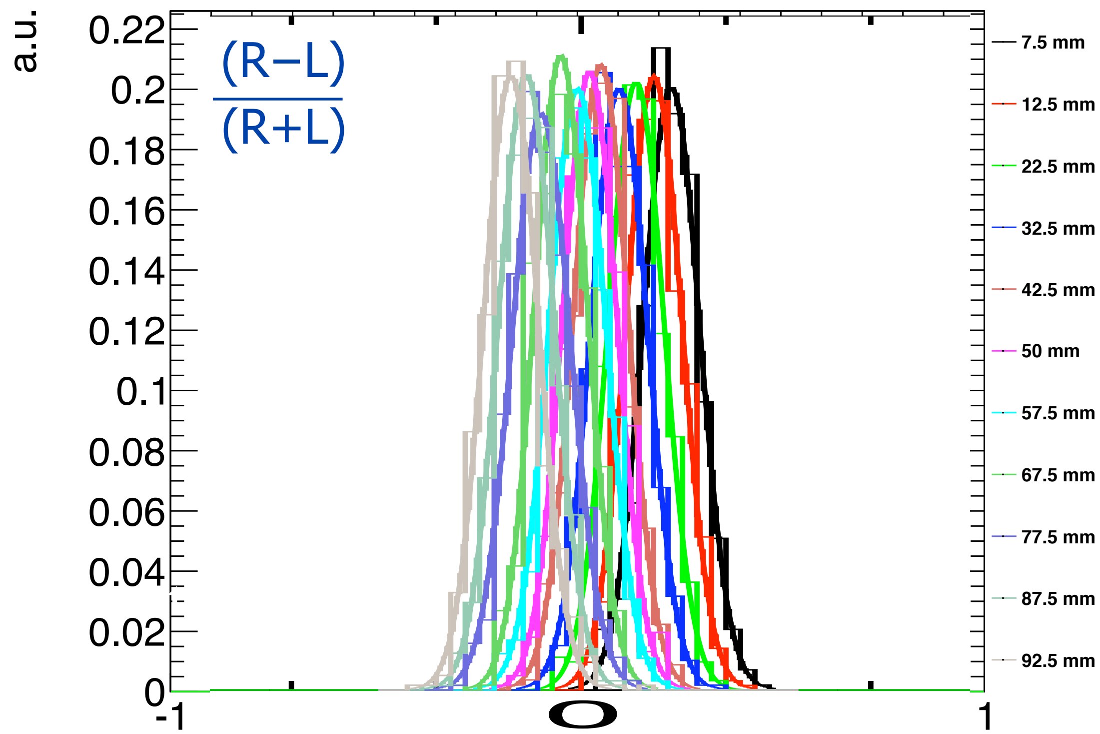
Axial coordinate of long dual sided readout crystal

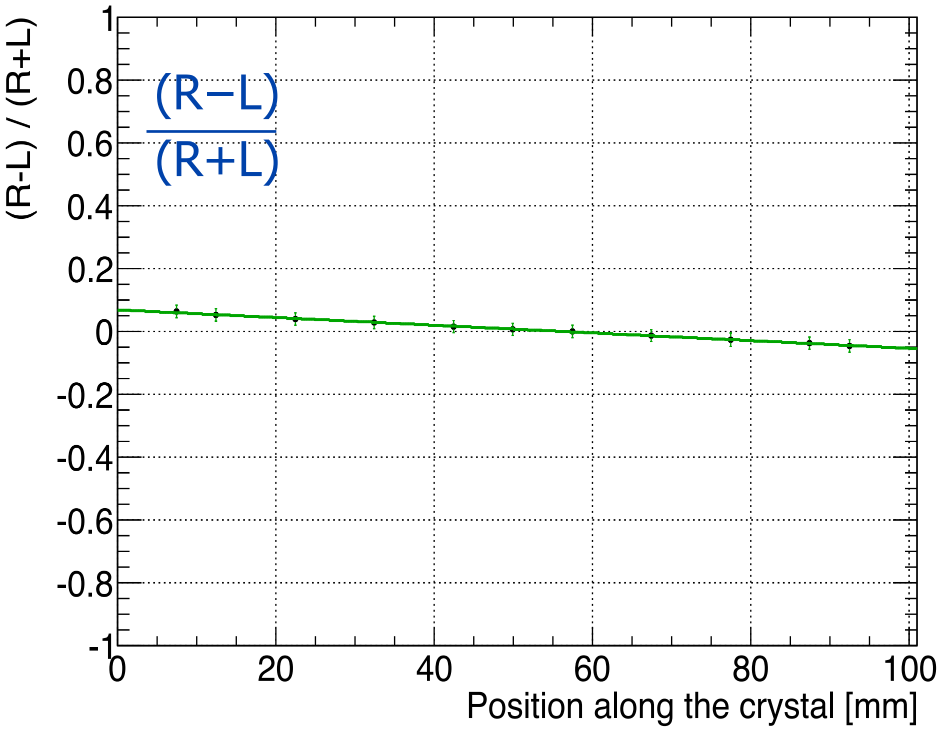
It doesn't work with standard AX-PET crystals (polished, clean surfaces) !

Detected **light yield** vs axial position



$\lambda_{optical}$ ~ 400 mm





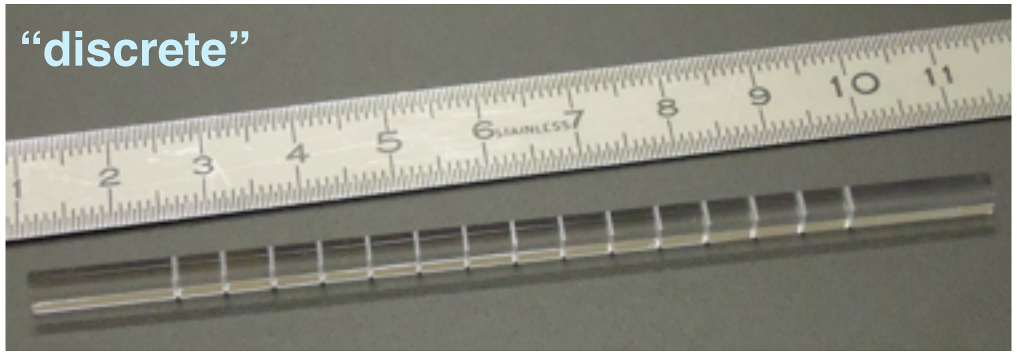
Destroying crystals...

Need to : - increase differences in the light yields L vs R
- artificially decrease $\lambda_{optical}$
- keep sufficiently high light yields

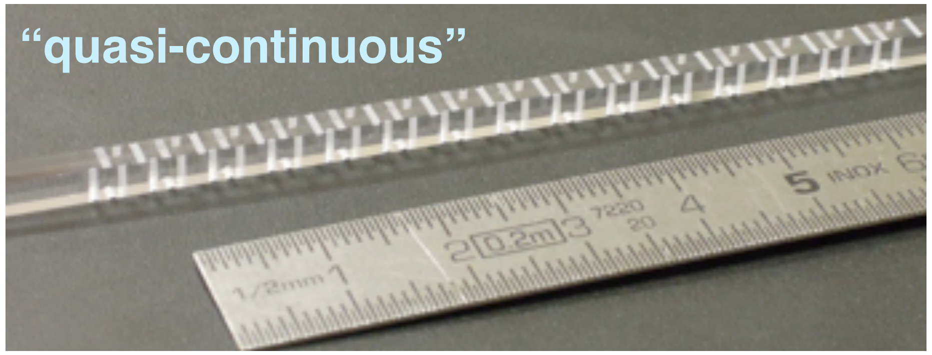
Empirical approach:

- surface treatment - polished crystals (from manufacturer)
- depolished 1 face, 2 faces (depolishing powder, grade 800)

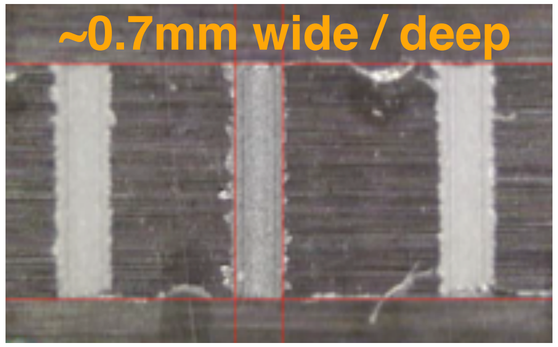
- mechanical CNC etching (diamond tool), 1 face, 2 faces, 4 faces



5 mm pitch, four faces identical



5 mm pitch, four faces staggered



@CERN DT division:
T. Schneider
M. Van Stenis
C. David

- wrapping
- bare
- teflon
- ESR Enhanced Specular Reflector, 3M

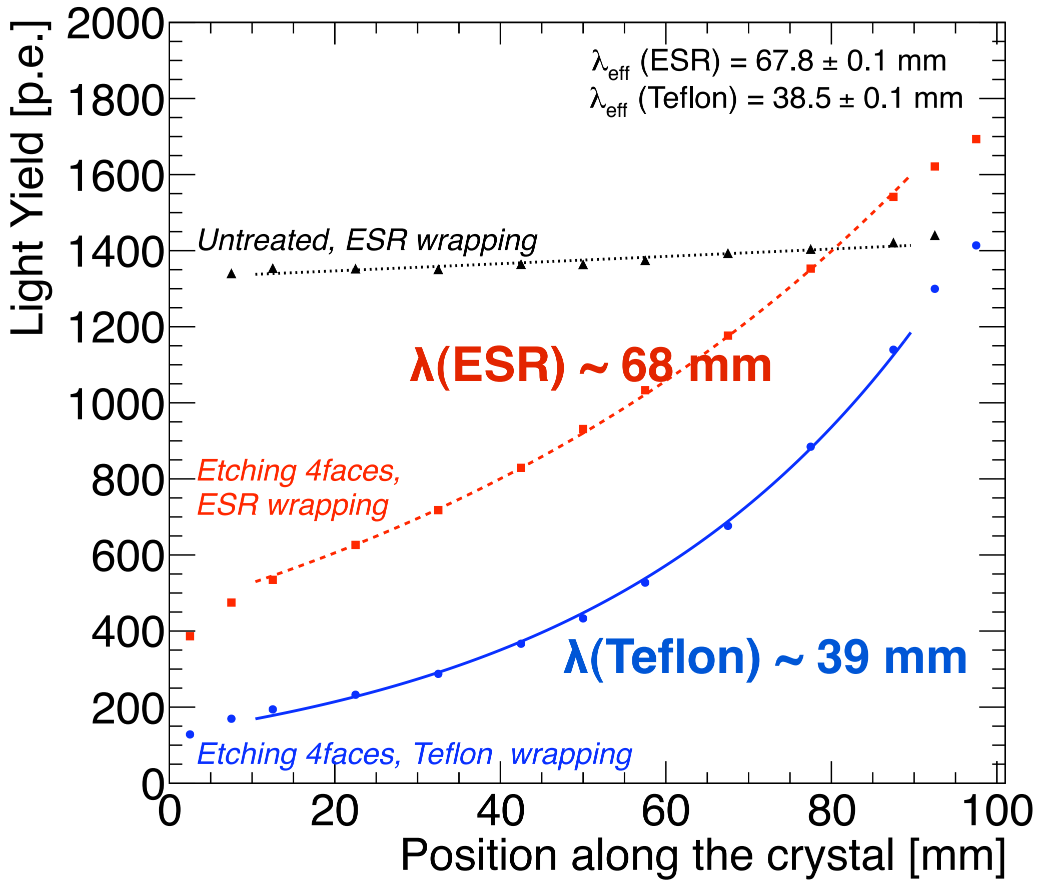
- (painted crystals)

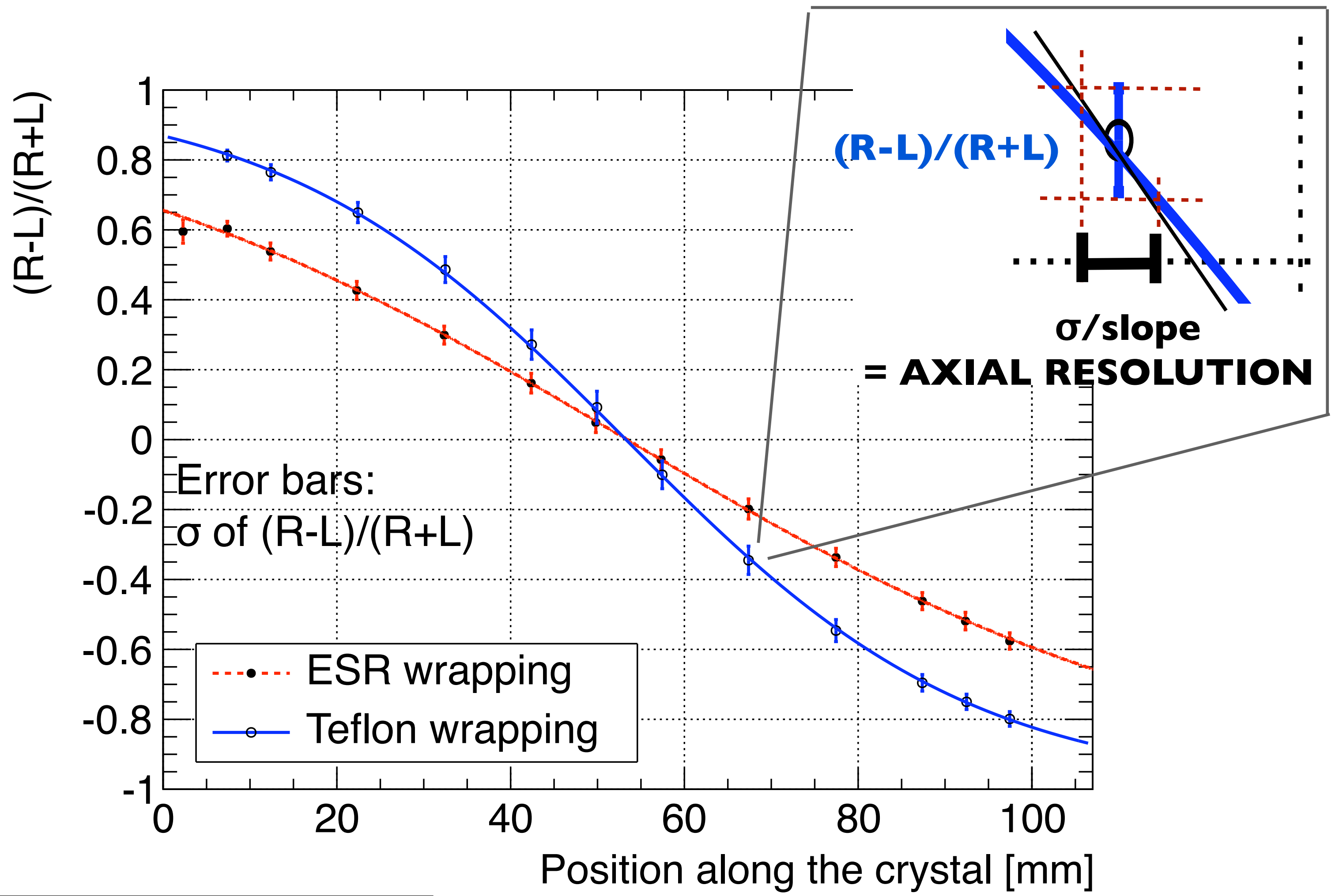
All combinations of surfaces / wrapping tested
Only the most significant results shown here

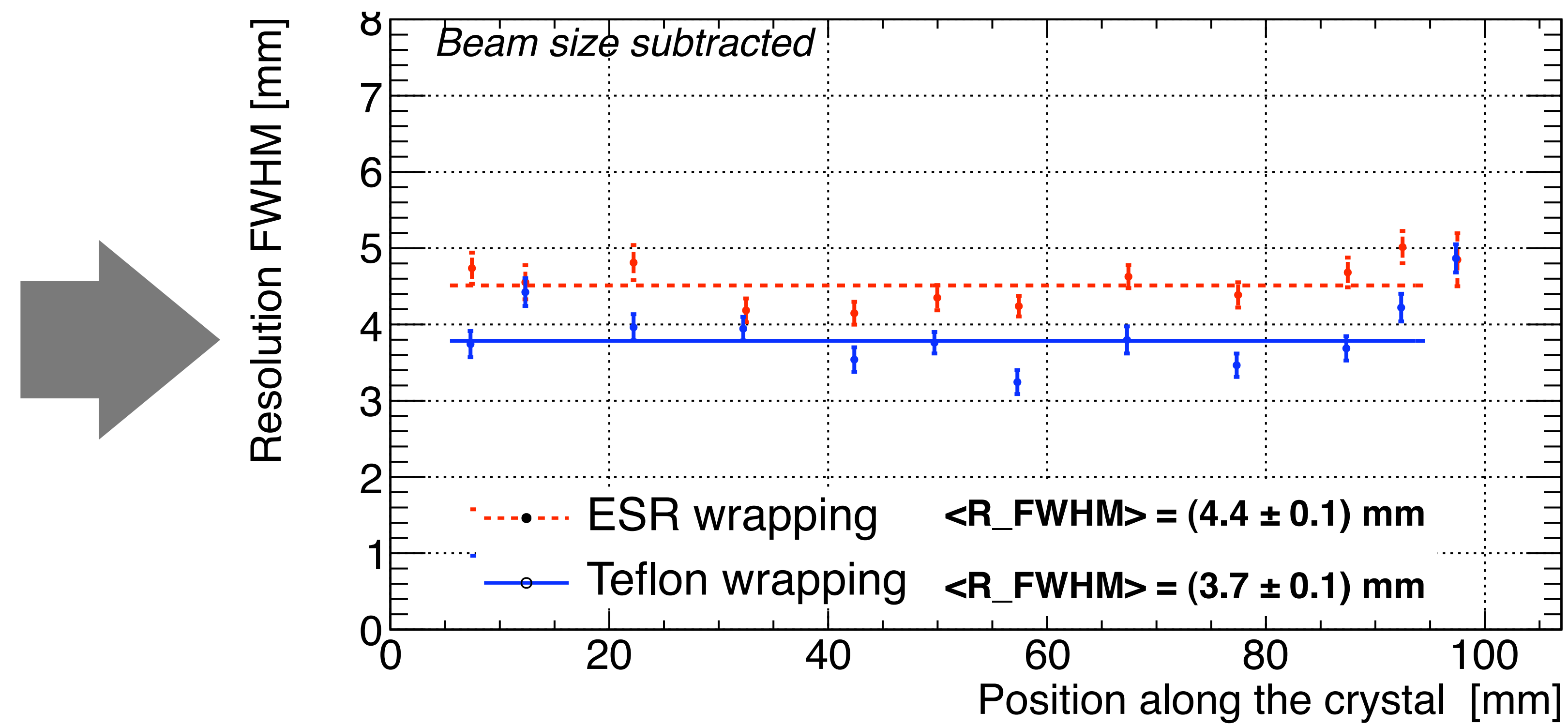
Mechanically etched crystal surface (staggered pattern)

representative of the general results

Detected **light yield** (one side)







Axial Resolution ~ 4 mm, FWHM

in agreement with simple Poisson-based statistical models
(given measured λ and LY)

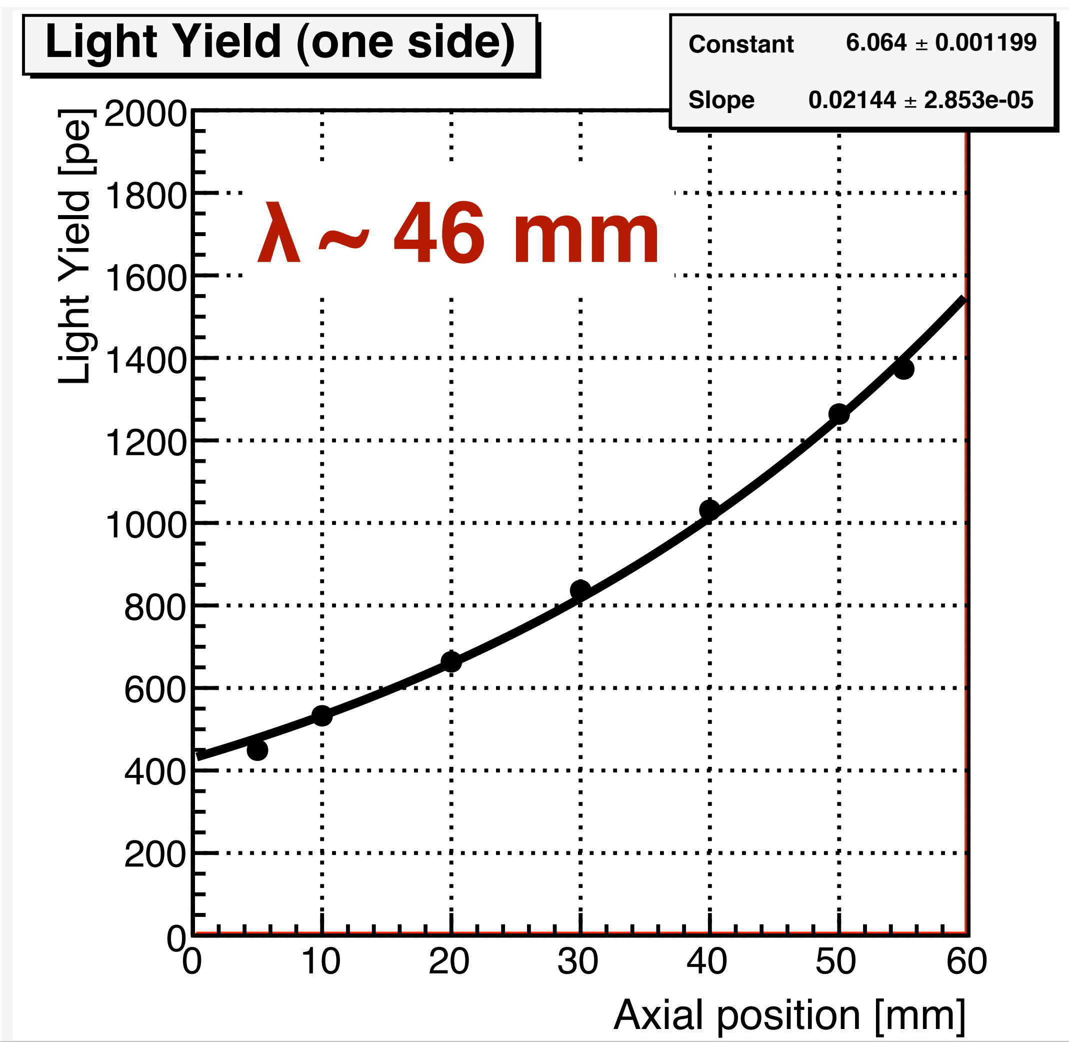
Additional test: 60 mm long LYSO crystals

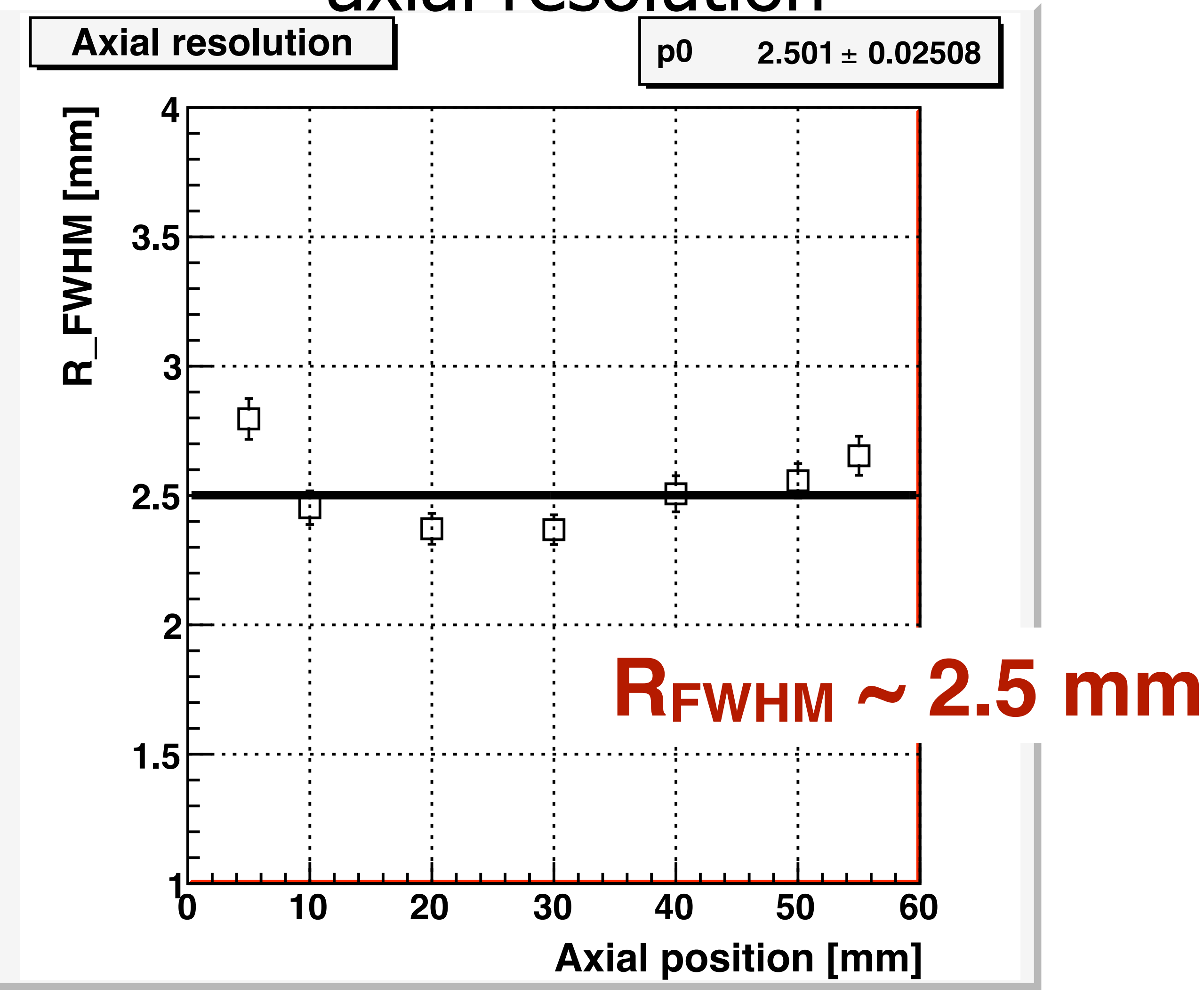
Preliminary !

NEW TESTED CRYSTAL

- **60 mm long crystal** [before: 100 mm]
- mechanical etching, 3mm pitch [before: 5 mm pitch]
- staggered 4 faces
- **Teflon wrapped**

axial resolution





very promising results with **60 mm long** LYSO crystals !

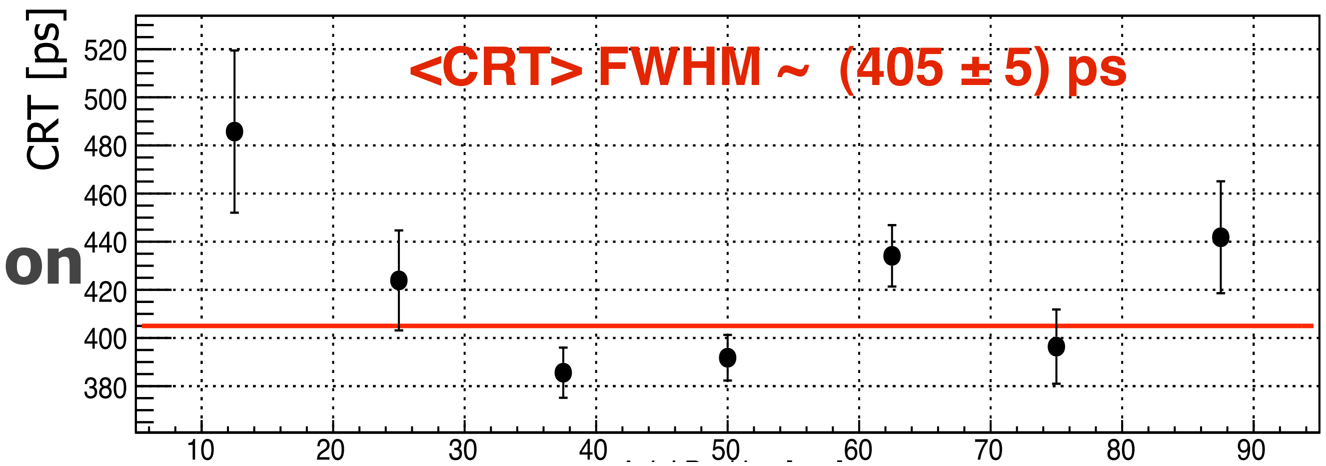
Timing performance of surface treated crystals

Preliminary !

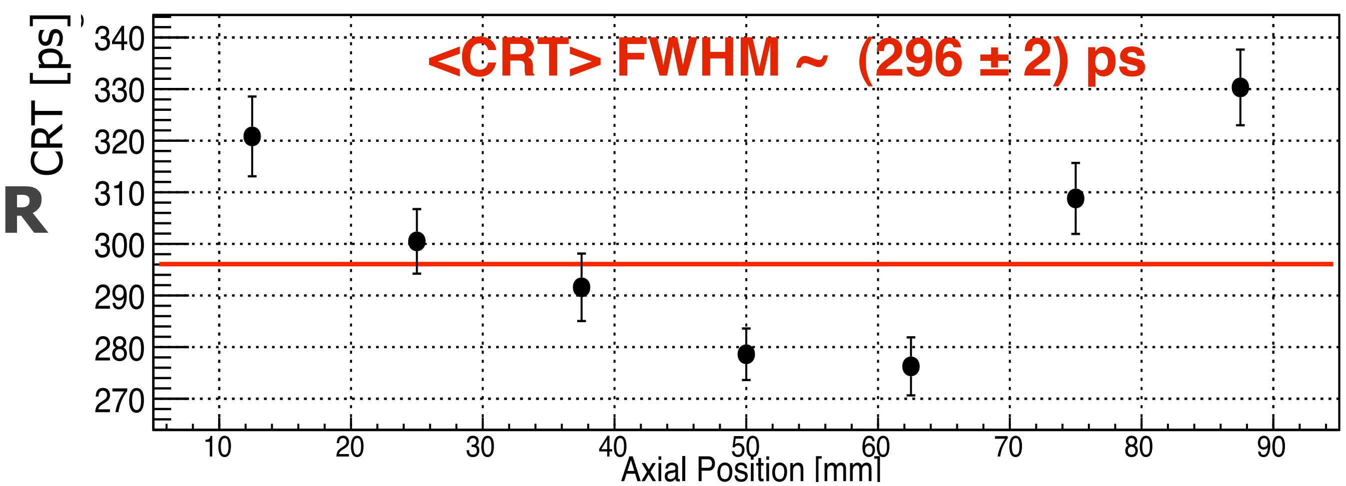
Which timing performance can be still achieved ?

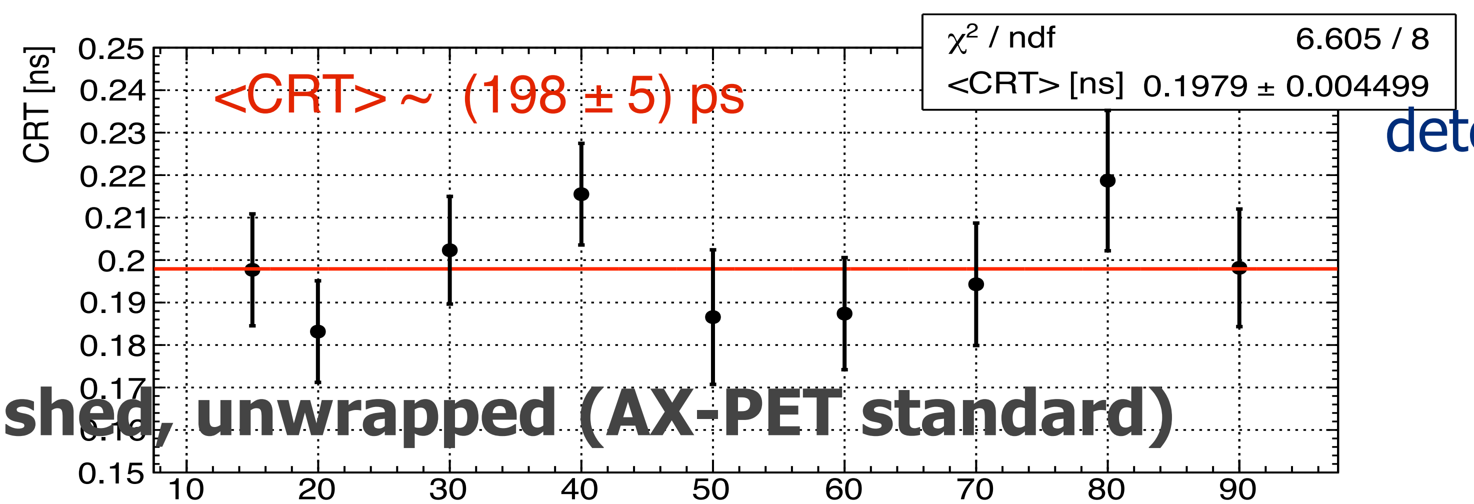
long crystal (t_ave) + tagging crystal

teflon



ESR





polished, unwrapped (AX-PET standard)

tested crystal: aligned etching,
4 faces, teflon/ESR wrapping

intrinsic resolution FWHM		computed two modules CRT (FWHM)
- polished	~ 149 ps	~ 211 ps
- treated surf, teflon	~ 383 ps	~ 542 ps
- treated surf, ESR	~ 266 ps	~ 376 ps
- 60 mm long, treated surf.	~ 215 ps	~ 304 ps

Surface treated crystals wrt polished crystals :

deterioration of the absolute timing resolution
non uniformity along the axial direction

not excellent but still acceptable
timing resolutions

Conclusions : AX-PET & beyond

Usage of 100 mm long axially oriented crystals for a PET :

(1) AXPET Demonstrator

- completed experiment
- excellent demonstration of the capabilities of an AXIAL PET for a high sensitivity / high resolution PET detector
- good detector performance demonstrated
  - **ΔE/E ~ 12%**
  - Axial Resolution ~ 1.35 mm (two modules coinc)
    => **Module axial resolution ~ 1.9 mm FWHM** (FWHM)
- good quality of reconstructed images for small animals (resolution, low contrast regions)

AX-PET
excellent axial resolution
(WLS solution from HEP)

(2) dSiPM readout of AX-PET standard (polished) crystals

- AX-PET performance confirmed
- Additional timing information :
  - dual sided readout, average timing => **CRT ~ 211 ps** (FWHM)
    => **Module timing resolution ~ 149 ps** (FWHM)

AX-PET + dSiPM
excellent timing resolution
towards AX-TOF-PET

(3) Dual sided readout of patterned surface axial crystals

- **Module(crystal) axial resolution ~ 4 mm** (FWHM)

Length of the crystal = **60 mm**
=> axial resolution ~ 2.5 mm (FHWM)

moderate spatial (and timing) resolution
compact, simple, highly integrated, high sensitivity
reduced number of channels
long axial FOV
only crystals in the FOV region
brain (MRI)PET ?

dreaming of an axial full ring PET detector...