



# The S-FIR experiment

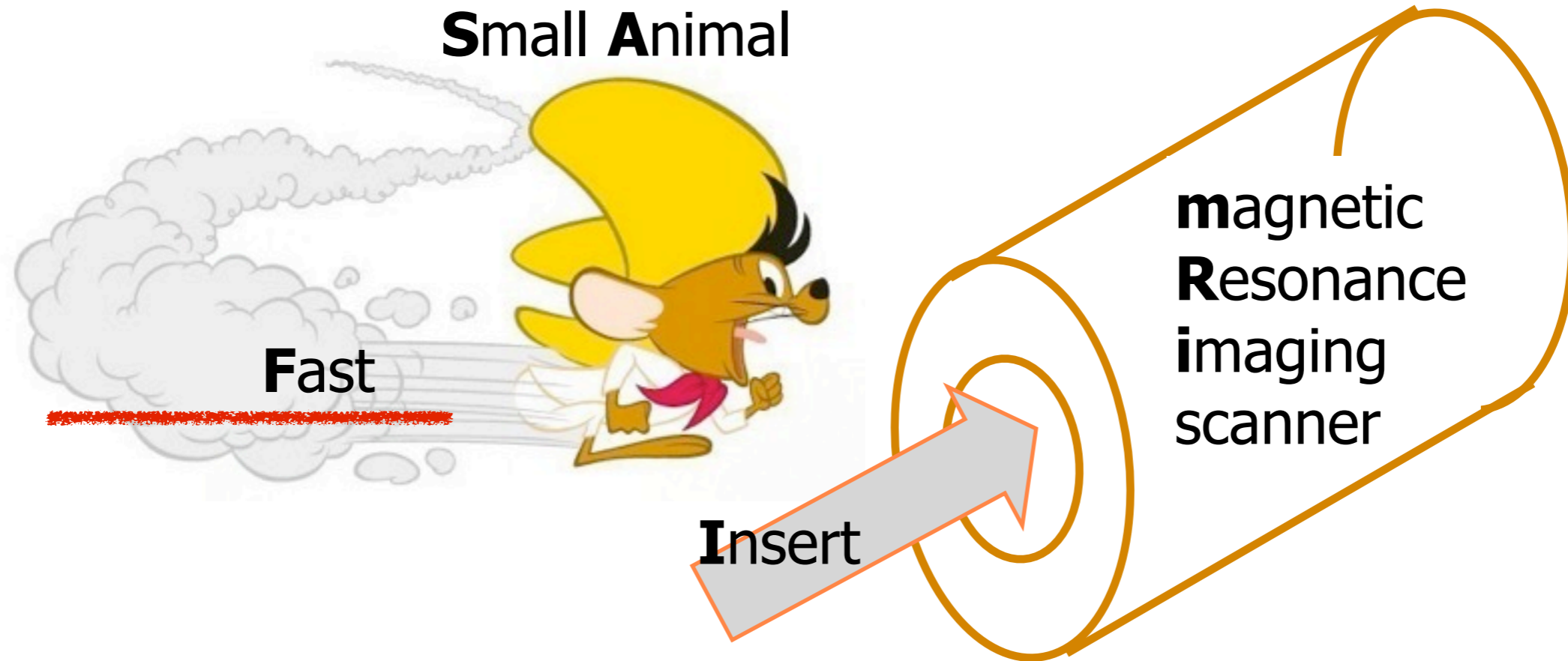
Chiara Casella  
IPP - ETH Zurich



ETH Institute for  
Particle Physics

UCL HEP seminar  
London, 26.02.2016

# SAFIR : Small Animal Fast Insert for mRi



R&D project in

**Positron Emission Tomography (PET)** instrumentation  
for pre-clinical **hybrid PET / MRI** acquisitions

# Outline

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## Define the context :

- PET basics
- multimodal PET/CT and PET/MRI
- short digression with a historical approach

## SAFIR :

- SAFIR goal
- detector design
- simulations
- image reconstruction
- characterization of the hardware components
  - SiPM
  - scintillator crystals
  - readout ASIC chips (high rate tests)
- future plans

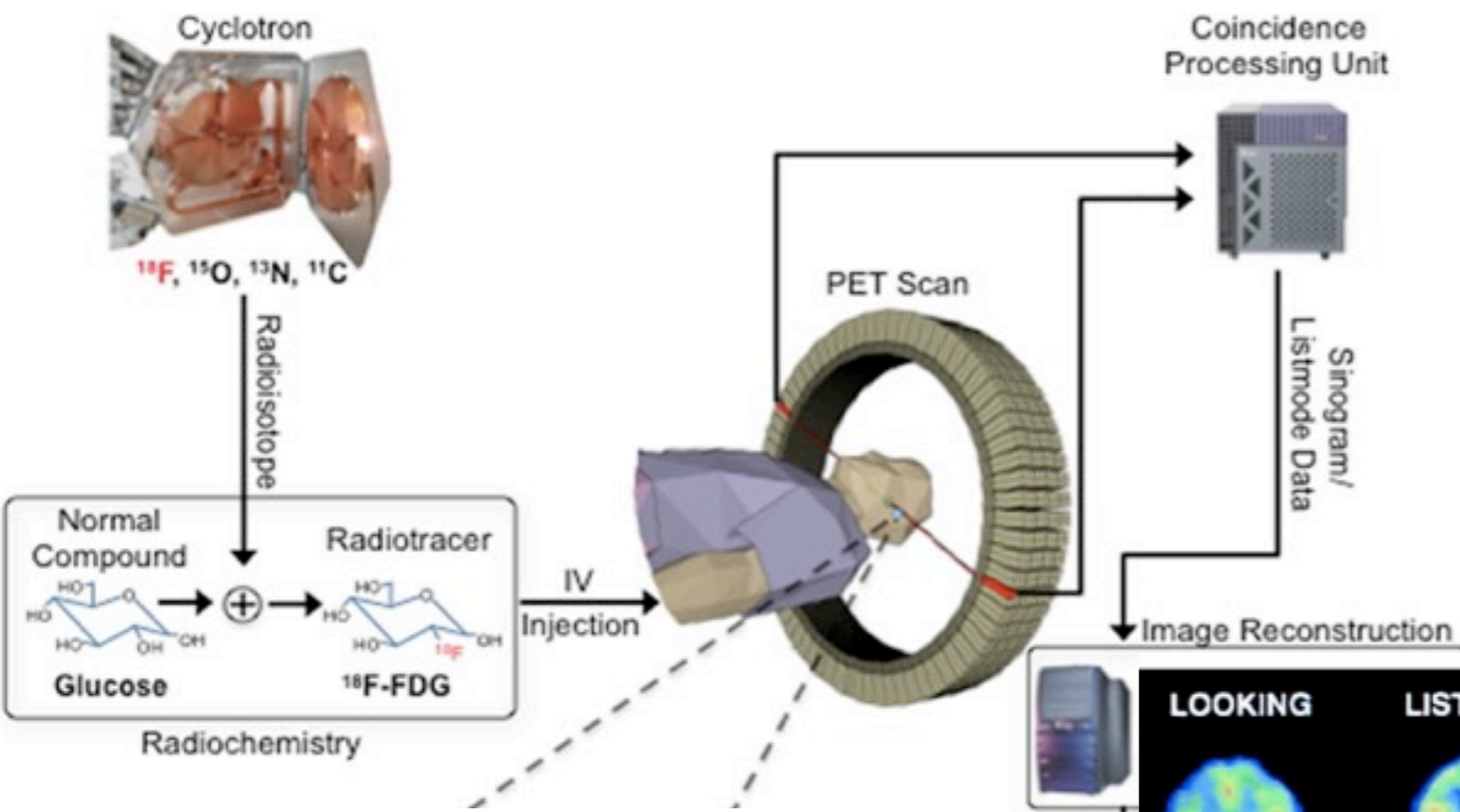
## Conclusions

A photograph of a stage with red curtains. The curtains are pulled back, revealing a dark stage floor. The lighting is dramatic, with the curtains being brightly lit and the stage floor being in shadow.

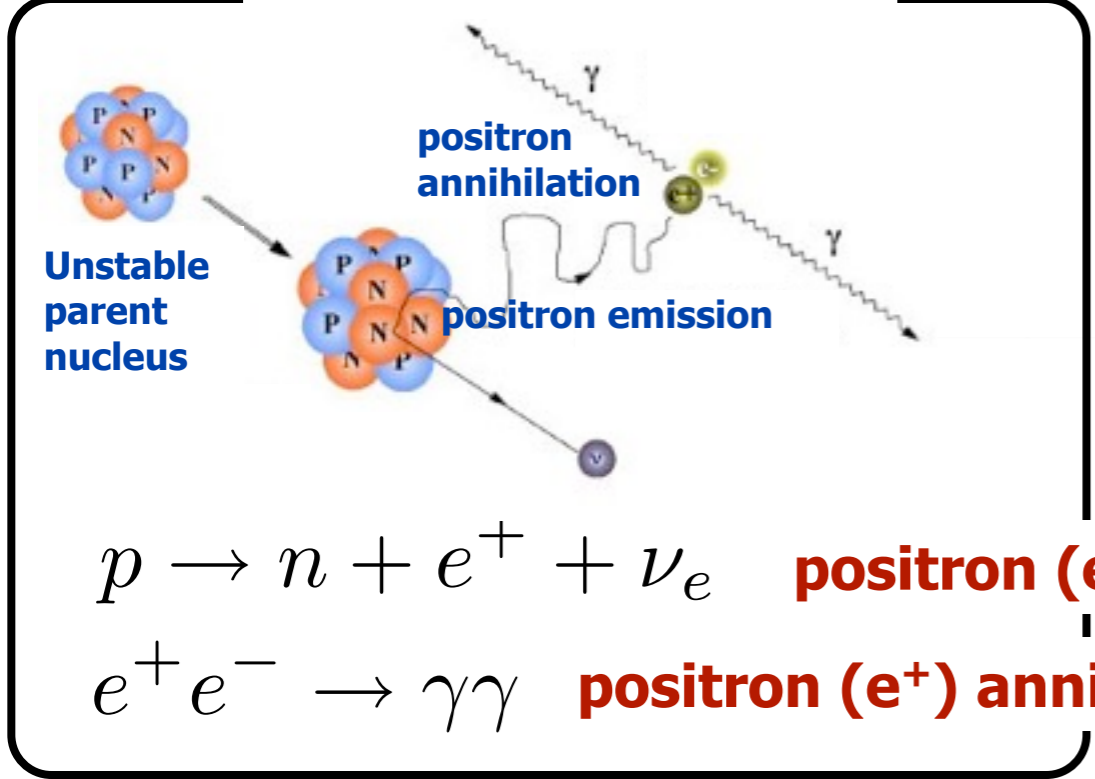
Setting the stage...

# PET : Positron Emission Tomography

nuclear medicine imaging technique for **in-vivo functional analysis**

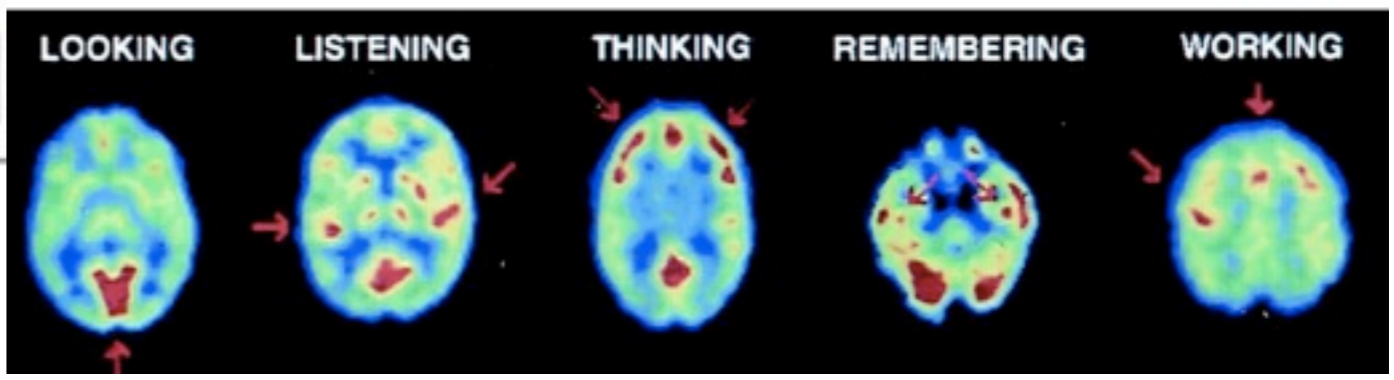


## PHYSICS PRINCIPLE



$$p \rightarrow n + e^+ + \nu_e \quad \text{positron ( $e^+$ ) emission : } \beta^+ \text{ decay}$$

$$e^+ e^- \rightarrow \gamma\gamma \quad \text{positron ( $e^+$ ) annihilation } \Rightarrow 2 \text{ collinear } \gamma \text{ photons of } E = 511\text{keV each}$$



map of the radiotracer concentration

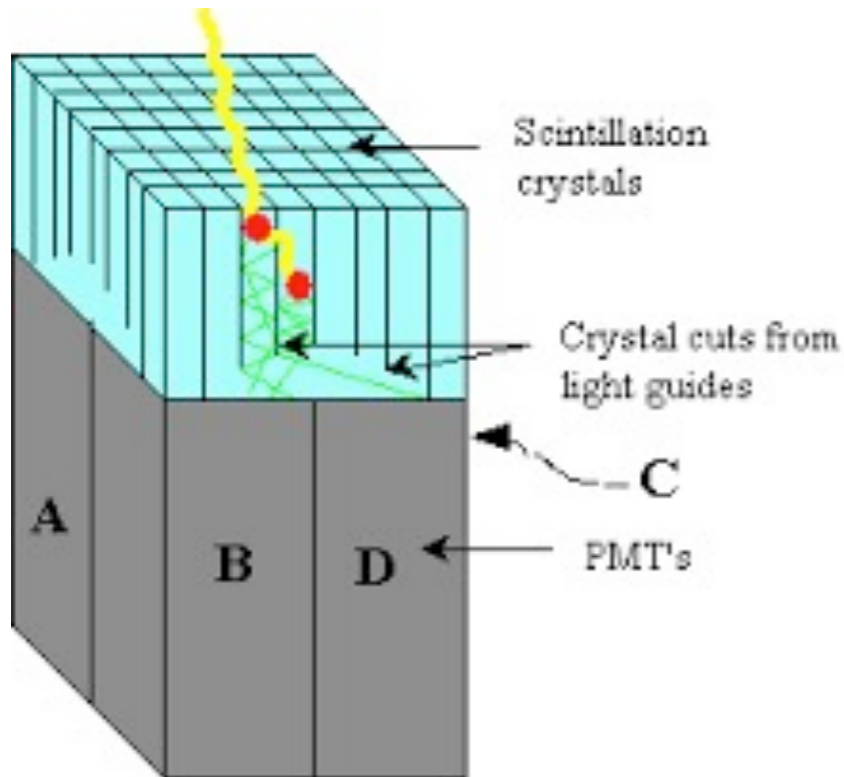
result : image of **functional processes** in the body

# PET detection principle

1. detection of 511 keV gamma photons
2. definition of coincidences

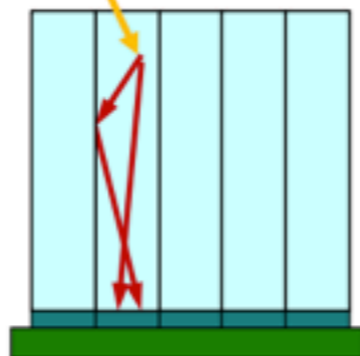
most widely adopted detection technique :

- **inorganic scintillators**  
mostly L(Y)SO [Lu based crystals]
- **photosensors**  
traditionally PMT (block detector)  
now Silicon based photodetectors (APD/SiPM)



## different approaches of xtal/photosensors coupling

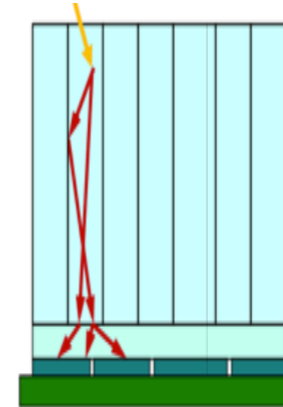
pixelated xtals  
**1:1 coupling**



good  $\Delta E/E$   
good time resol.  
large signals

CLINICAL

pixelated xtals  
**+ light sharing**  
=> Center of Gravity



high spatial resol.  
small signals  
increased data rate

PRE-CLINICAL (small animals)

**monolithic**  
=> Center of Gravity



higher spatial resol.  
smaller signals  
largest data rate

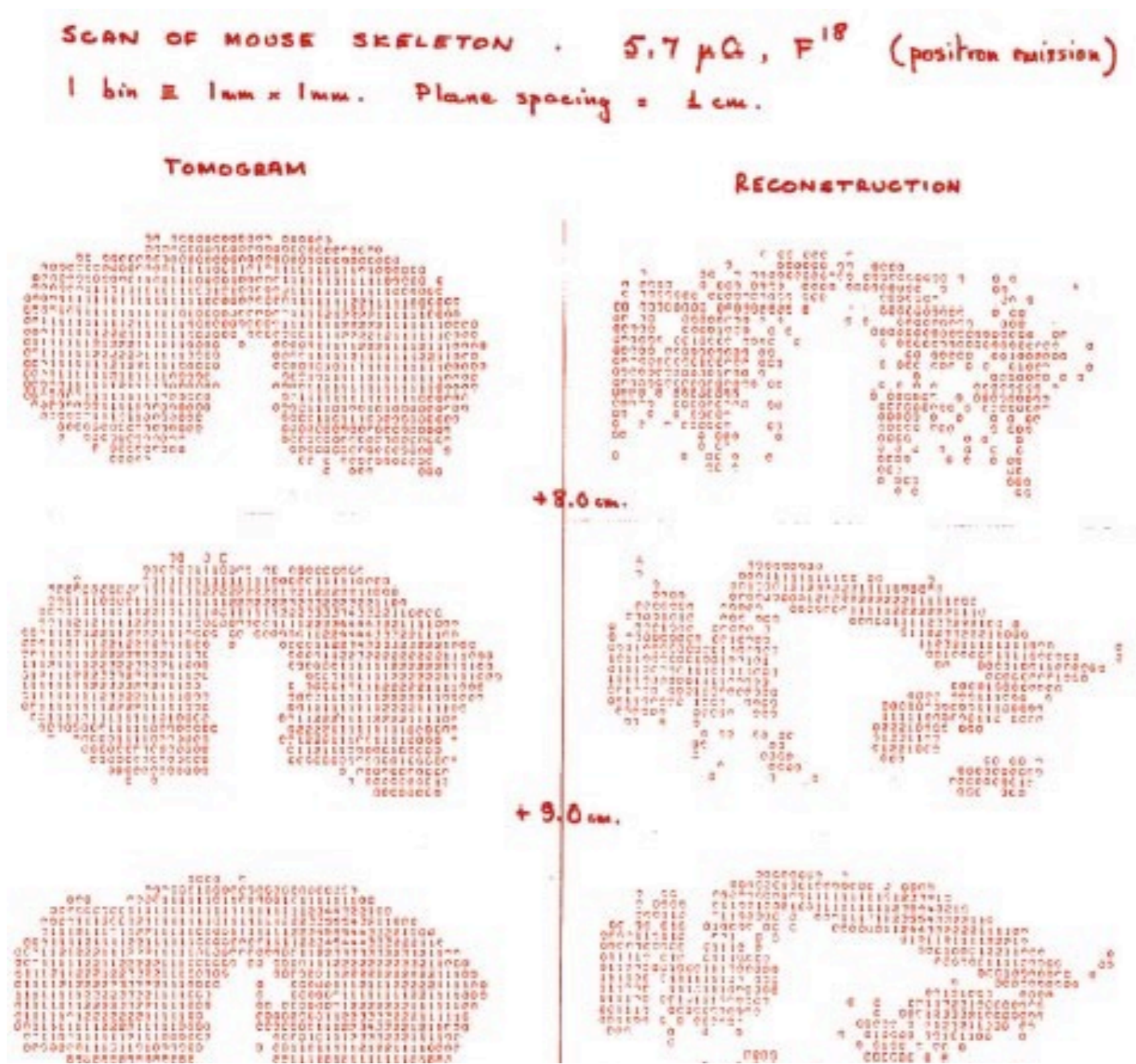
**BLOCK DETECTOR configuration**

# Early PET images (at CERN)

D. Townsend, A. Jeavons  
**CERN, 1977**

first reconstructed image  
of the skeleton of a  
mouse injected with 18-F

detector :  
HIDAC i.e. wire chamber  
(from G. Charpak)

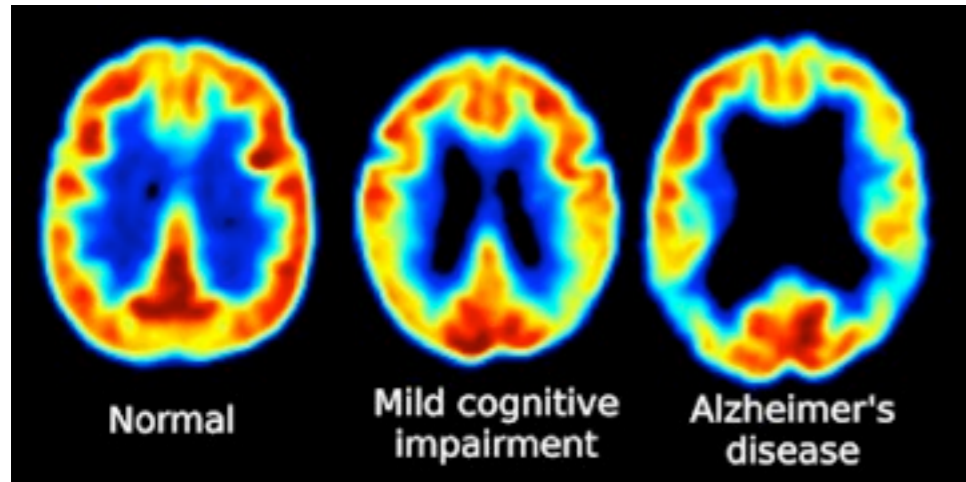


“You are indeed correct that the birth  
of PET is somehow controversial”  
(D. Townsend)

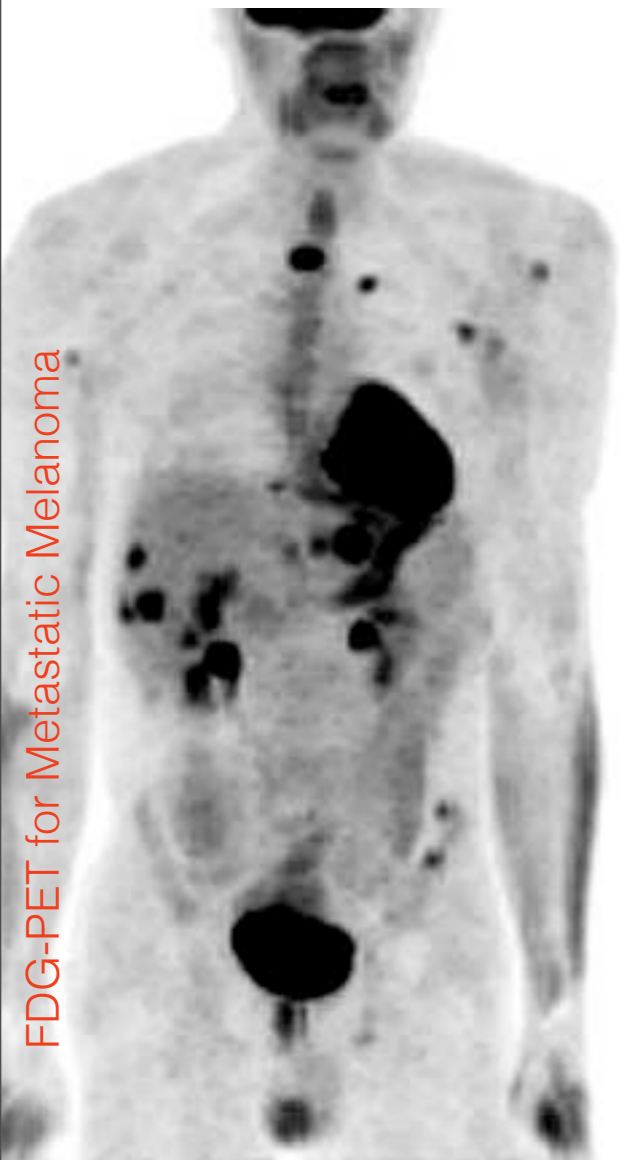
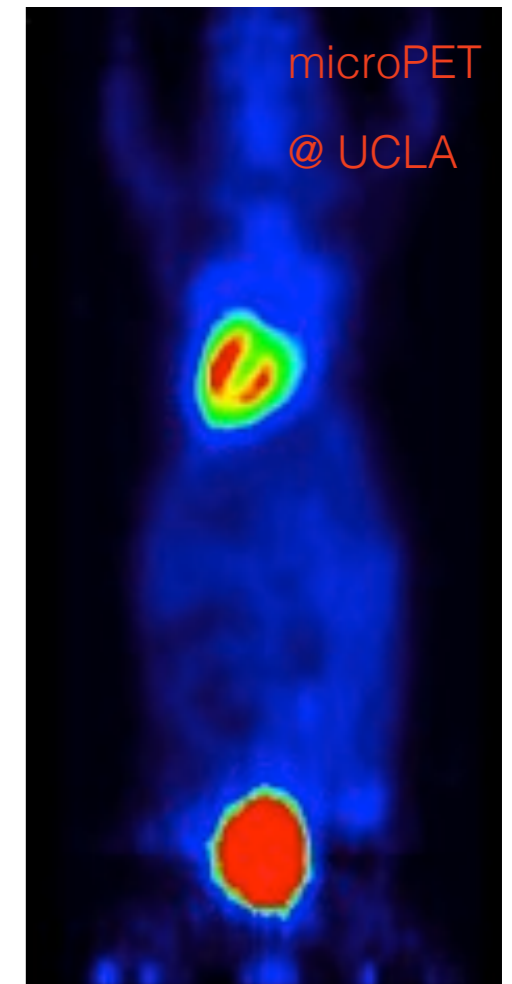
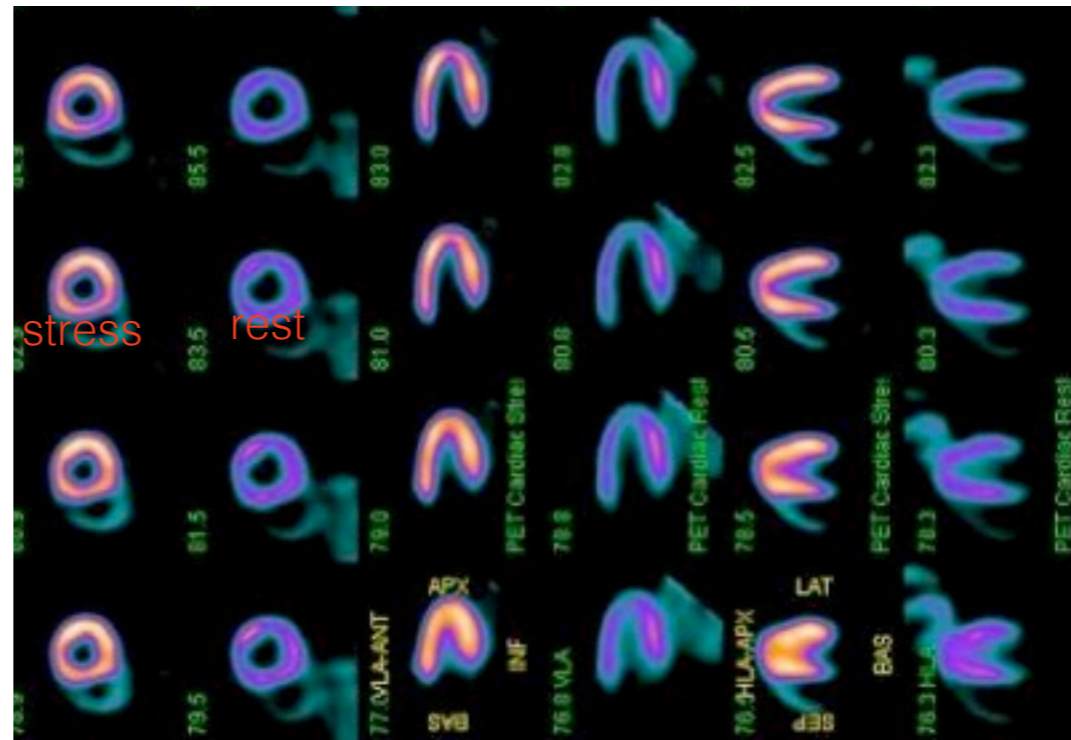
RAW DATA RECORDED  
IN THE DETECTORS

RECONSTRUCTED  
IMAGES

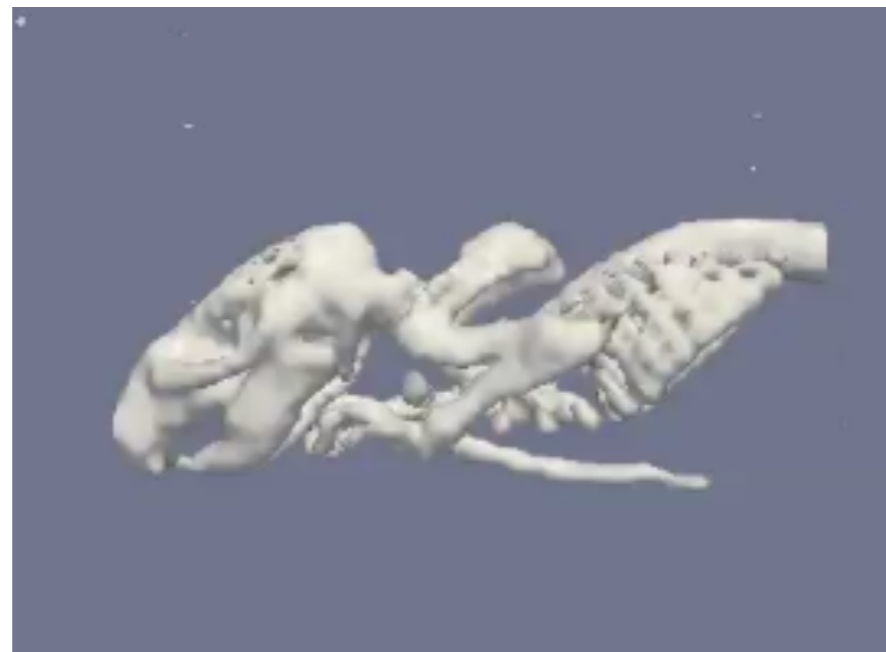
# Randomly selected PET images



myocardial perfusion (Rb-82) in a normal patient



F-18 young rat imaged with the AX-PET



## huge domain of applications

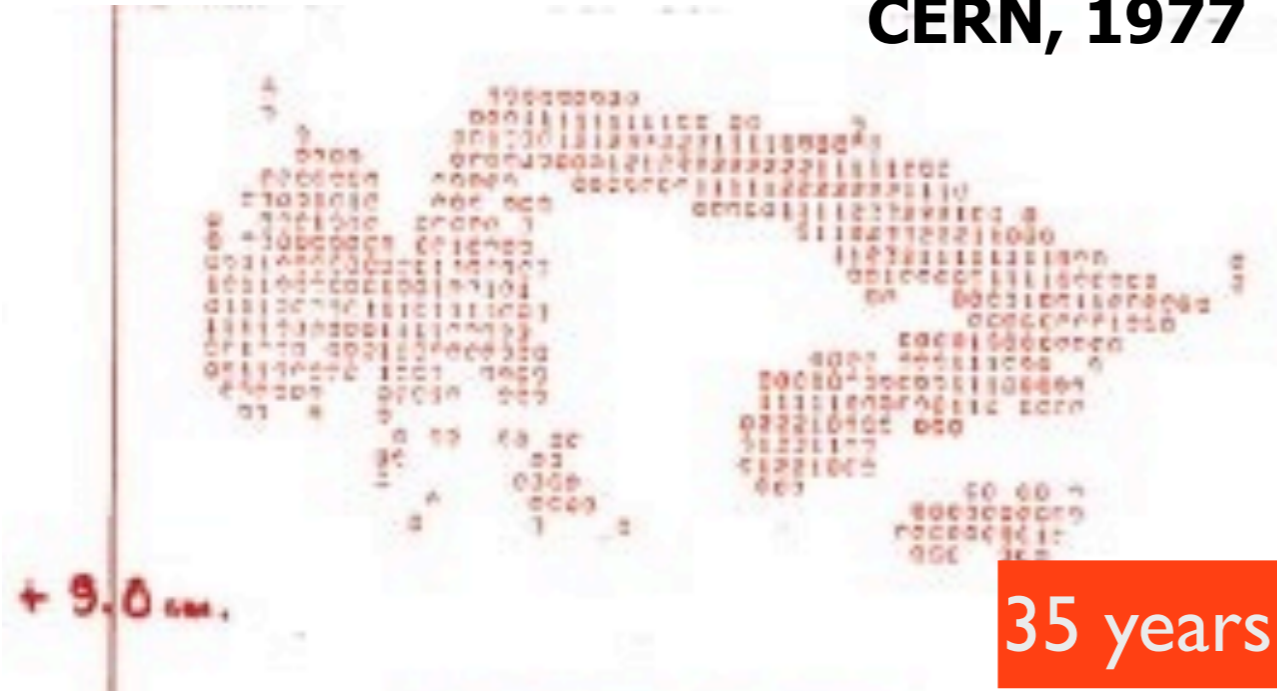
both in **clinical** and **pre-clinical** fields

- full body / brain /or organs-specific
- oncology (diagnosis, tumor staging)
- study of neurodegenerative diseases
- psychology
- cardiac functioning monitoring
- in-beam monitoring in hadron-therapy
- medical research
- pharmacokinetics
- development of new tracers
- ...



# Skeleton of a mouse injected with 18-F at CERN

D. Townsend, A. Jeavons  
**CERN, 1977**



AXPET experiment  
**CERN, 2012**



35 years later...

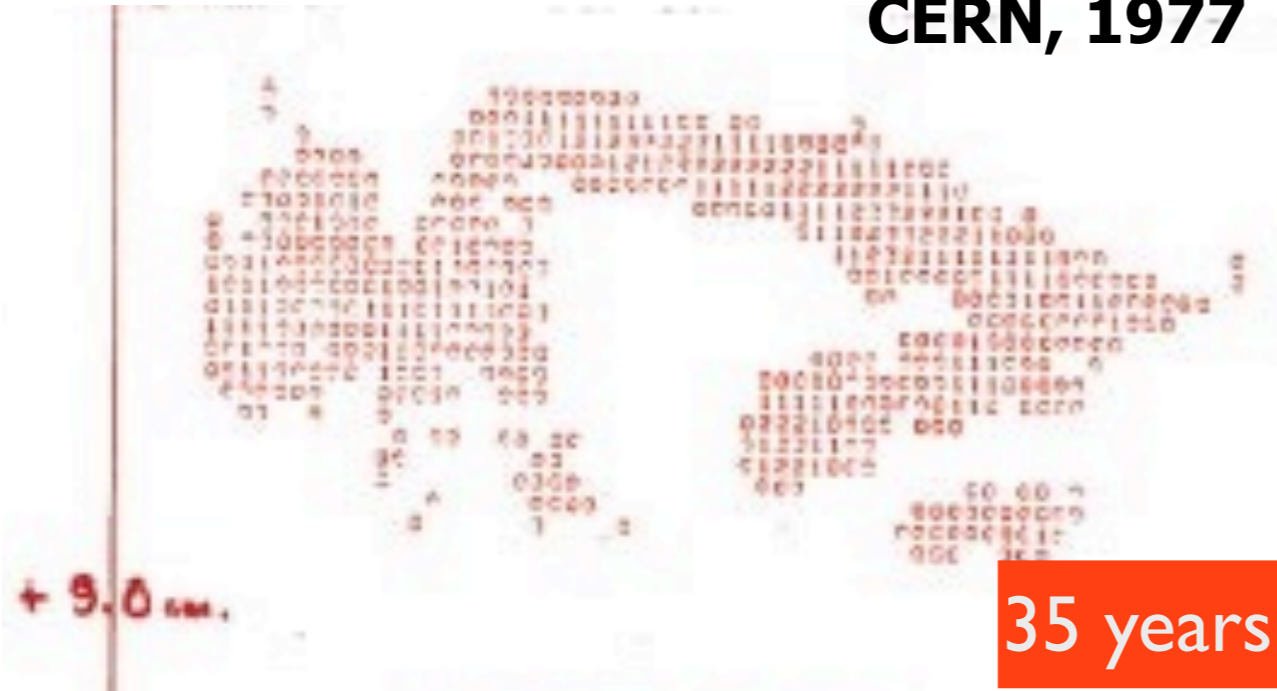
**remarkable development!!**

Most important factors that contributed to this :

- **instrumentation development** [great boost from HEP : calorimetry / new crystals / new photodetectors / electronics ]
- **computing power** [improved reconstruction algorithms]
- **radio-chemistry** [FDG-based radiomarkers]
- **PET / CT** (Computed Tomography)

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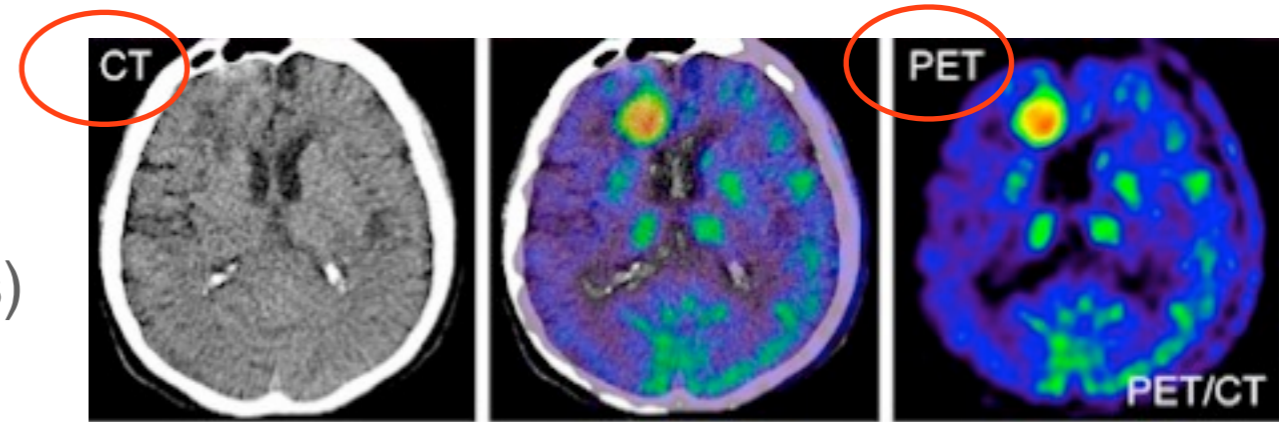
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# PET and CT: a perfect fit

- idea: combine **functional imaging from PET** with **morphological imaging from CT** (X-rays) (D. Townsend)
- born in the clinical domain (first commercial PET/CT scanner: 2001)
- 2006 : no more stand-alone PET !

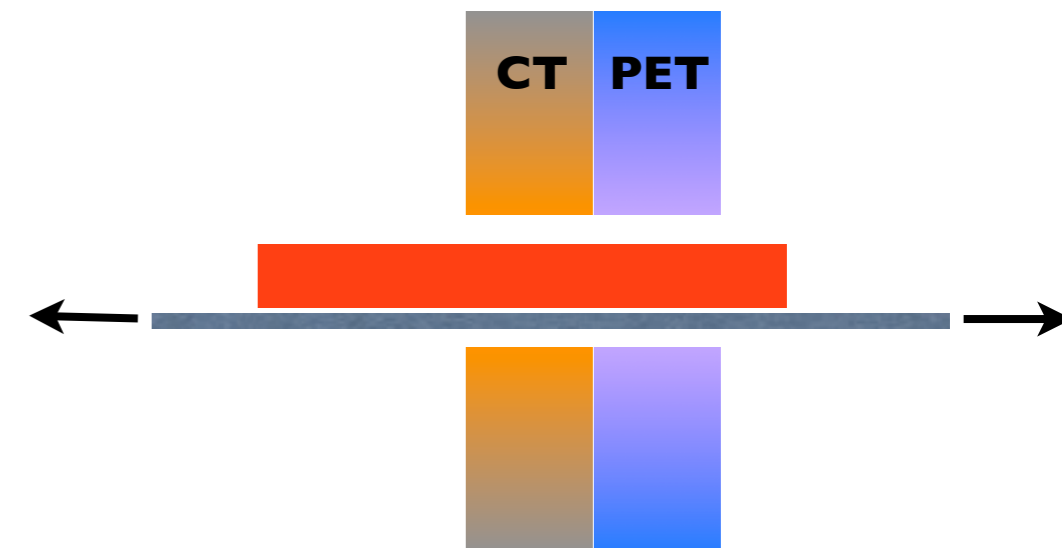


## A revolution in medical imaging !

- clinical evaluation (~ 10 years) => **importance of co-registered anatomical information at high resolution with functional data**
- immediately recognized by-product :
  - CT generates the attenuation correction map needed for PET to be quantitative (instead of lengthy transmission scans)

### PET/CT :

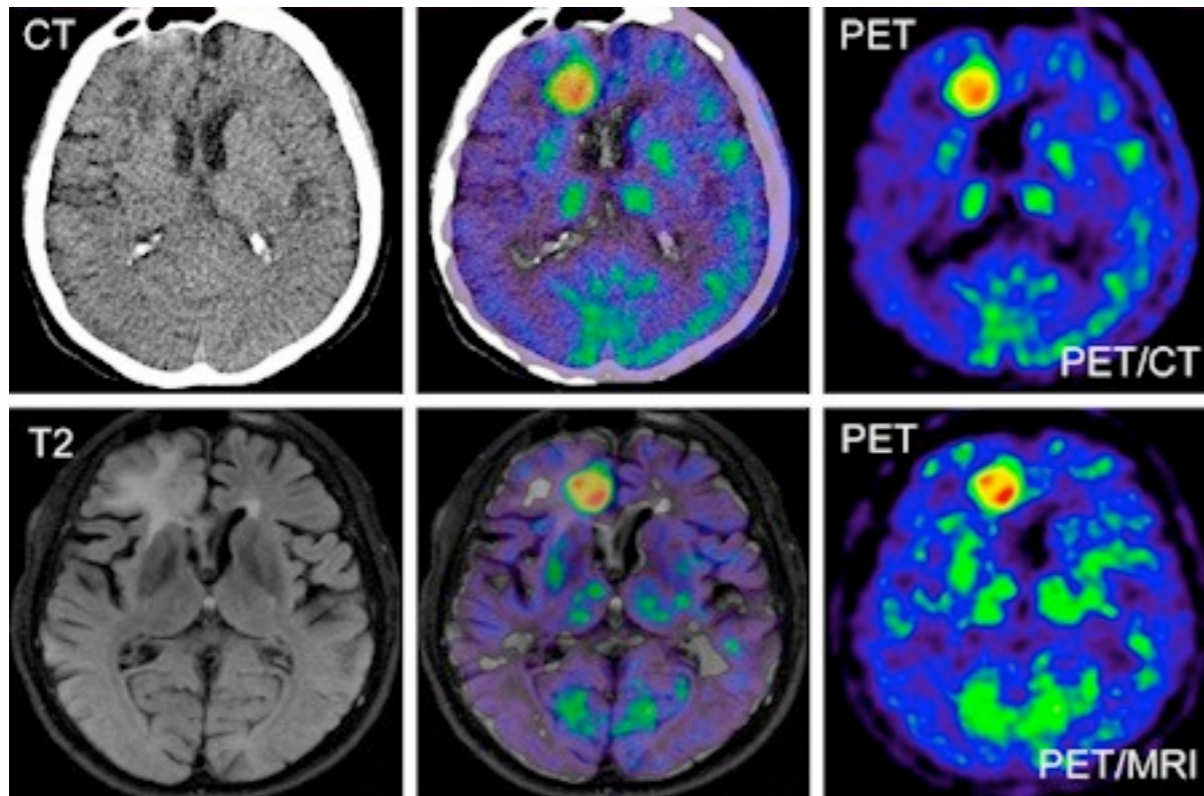
- Localization
- CT-based attenuation correction



- the 2 devices mounted sequentially (essentially unmodified) in a common gantry
- translational patient bed

# PET and MRI: an even better fit ? - PART I

MRI : **M**agnetic **R**esonance **I**maging also provides morphological information



Anatomical counterpart for PET:

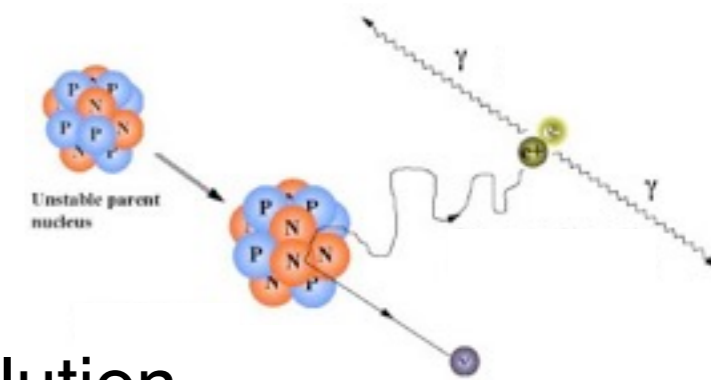
CT

or

MRI ?

## Advantages of PET/MRI vs PET/CT :

- high soft-tissue contrast (brain)
- no additional dose (kids)
- reduction in positron range => improved spatial resolution
- possibility of simultaneous acquisition  
=> no temporal mismatch (organs movements)



# PET and MRI: an even better fit ? - PART II

MRI is also **functional** - full complementary to PET

**Two examples :**

## [1] MRS (Magnetic Resonance Spectroscopy)

- study tissue metabolism with  $^{13}\text{C}$ -labelled substrates
- MRS: high chemical specificity in identifying different metabolites
- MRS: low sensitivity (or interference with metabolism processes)

if  **$^{11}\text{C}$**  -labelled => **MRS + PET**

## [2] CBF - Cerebral Blood Flow

- importance of constant delivery of oxygen in the brain
- CBF mechanisms are not yet completely understood
- CBF used as surrogate of neural activity in MRI => functional MRI

if  **$^{15}\text{O}$** -H<sub>2</sub>O => **fMRI + PET**

$t_{1/2}(\text{O-15}) \sim 2$  mins

changes of CBF up to 20% in time scales of seconds

=> high temporal resolution needed

# Hybrid PET / MRI

Great potential for PET/MRI to become the dominant nuclear imaging technique

- **MRI as the anatomical counterpart of PET** (with advantages wrt CT)
- **Functional capabilities of MRI (fMRI)**

**1 + 1 > 2!**

The potential of PET/MRI is fully exploited when :

- **fully simultaneous** (time / space correlation) => **PET inside** the MR bore
- **dynamic studies**

**But...**

**PET / MRI is technically very challenging !**

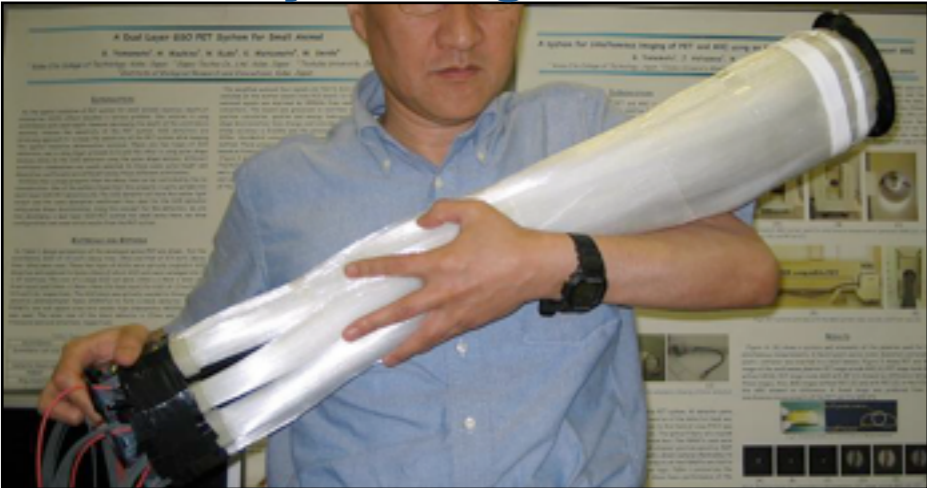
- **Mutual non-interference of the two modalities**
  - PET must work into MRI (no PMT ; heating / vibrations; electronics interference)
  - MRI must be undistorted by PET
- **Limited space available**

**difficult, but possible**

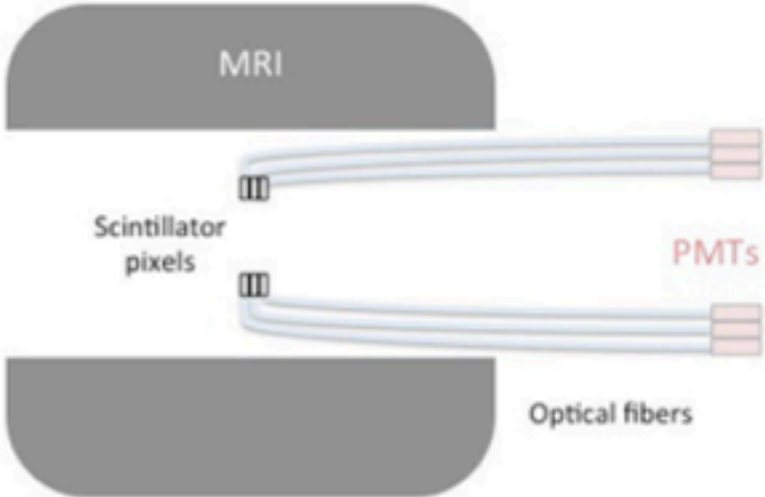
# Possible, thanks to the revolution in photodetection

**PMT**  
high gain  
good timing  
not MR compatible

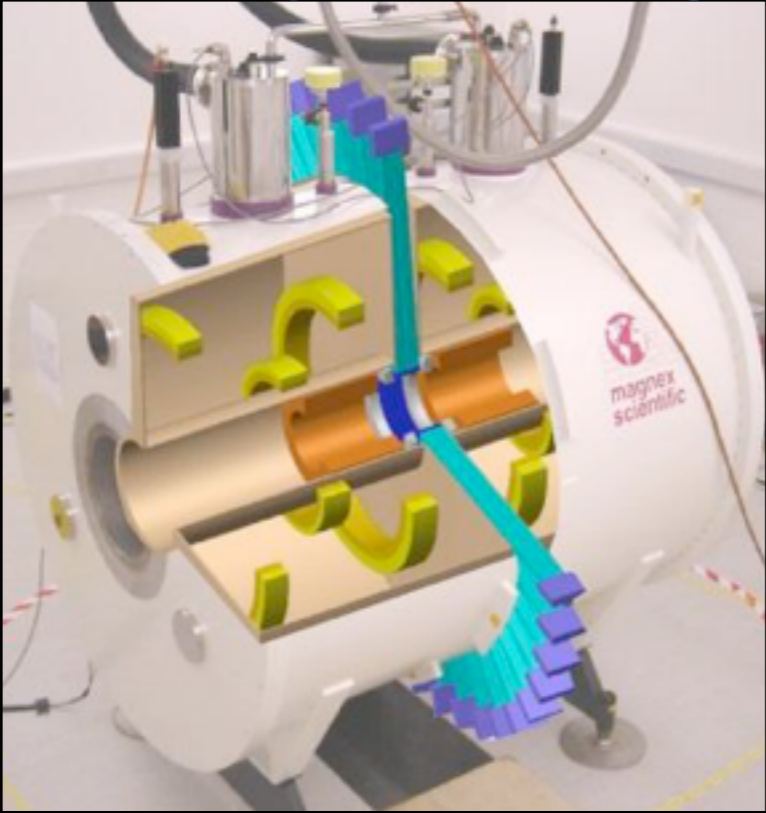
## Kobe City College, Osaka University



fibers + PS-PMT  
Axial  $\sim 0.5$  cm



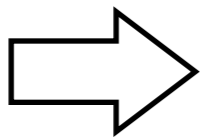
## University of Cambridge



split magnet  
fibers + PMT  
Axial  $\sim 7$  cm

# Possible, thanks to the revolution in photodetection

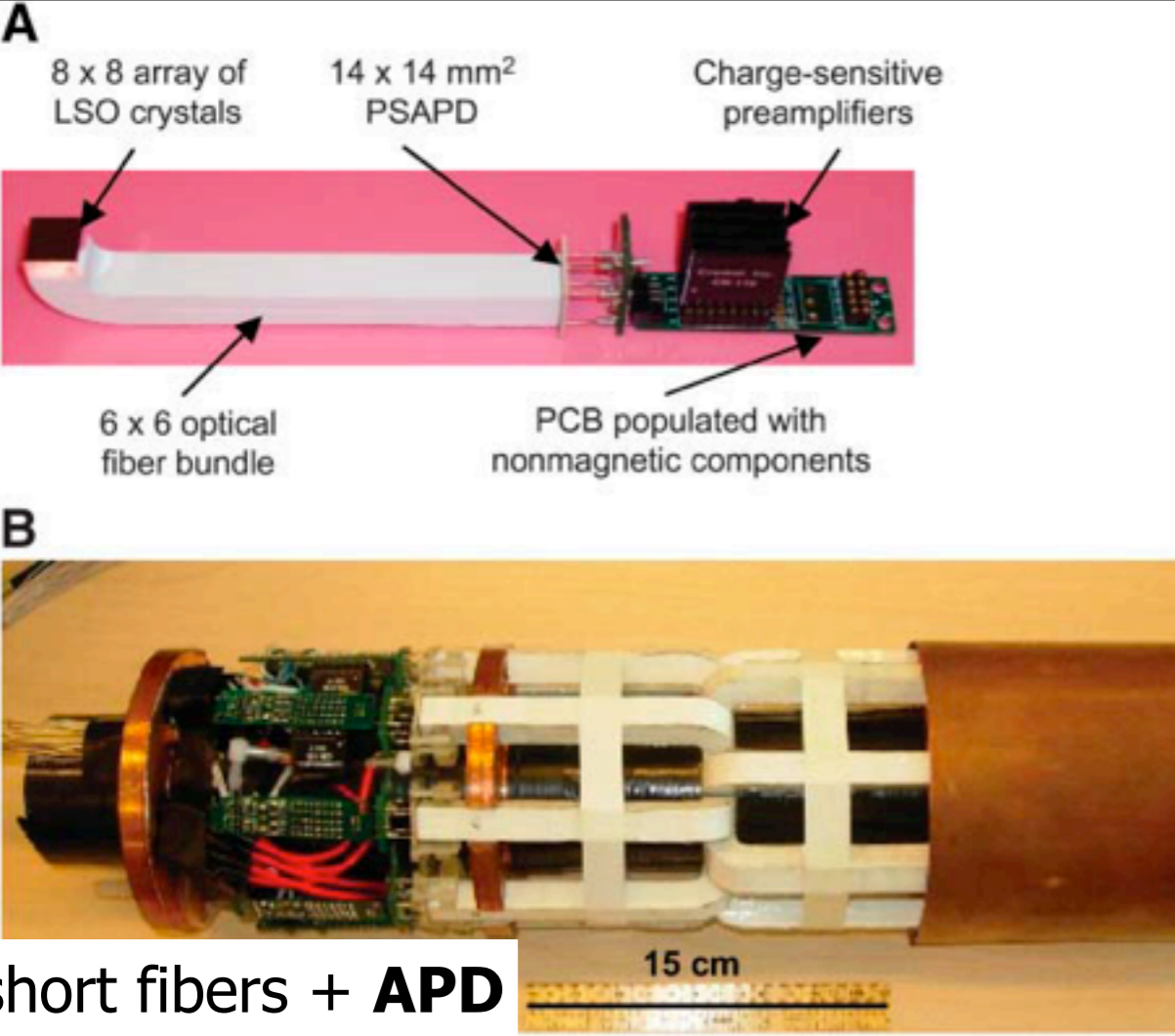
**PMT**  
 high gain  
 good timing  
not MR compatible



**APD (Avalanche Photo Diodes)**  
 insensitive to magnetic field / compact /  
 low gain  
 => worse timing perms  
 => need of very low noise FE electronics

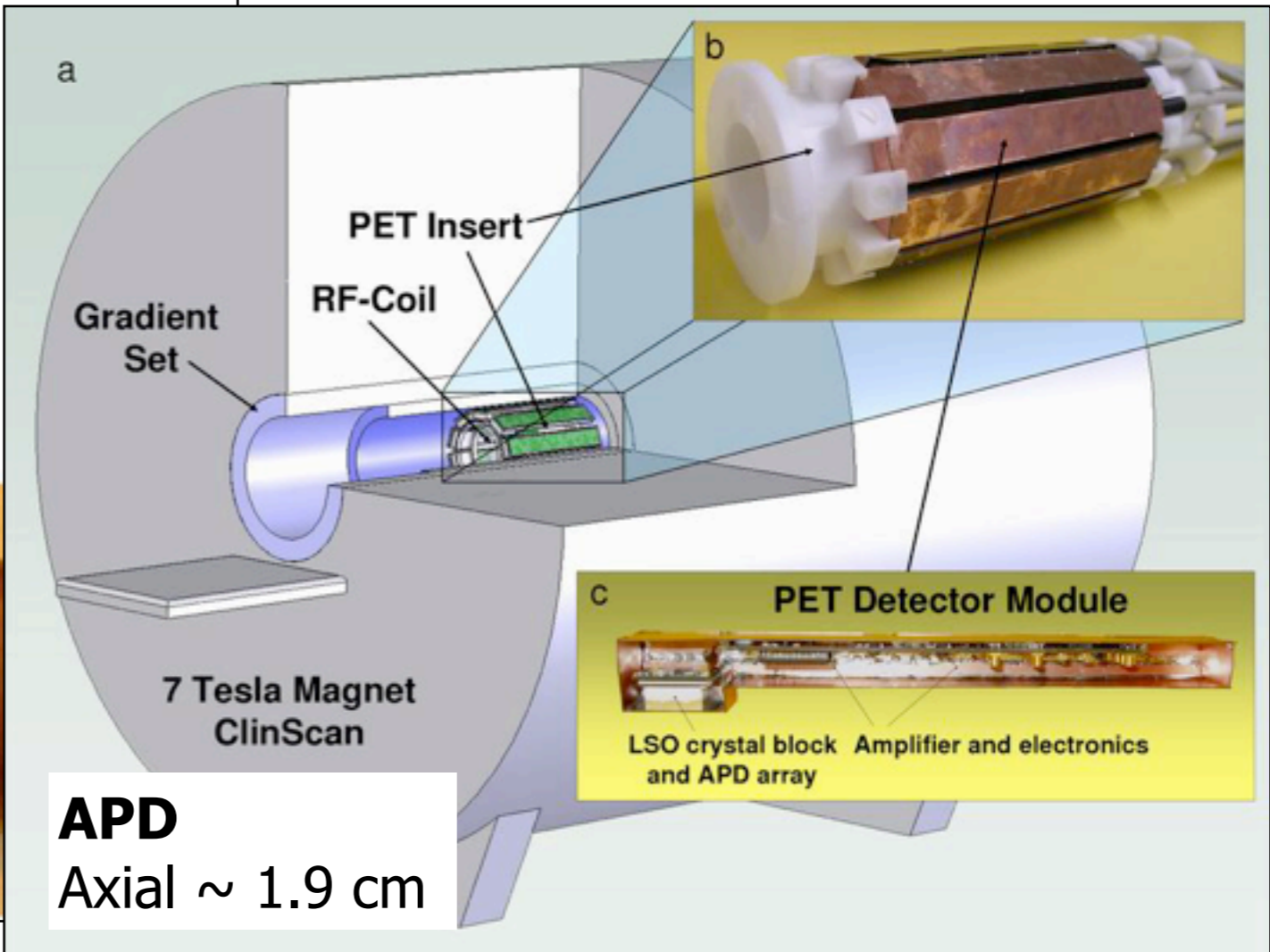
relevant examples of **pre-clinical simultaneous** PET/MRI that have been used for **in-vivo analysis**

## UC Davis, California



short fibers + **APD**  
 Axial ~ 1.4 cm

## University of Tuebingen, Germany



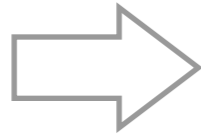
**APD**  
 Axial ~ 1.9 cm



# Possible, thanks to the revolution in photodetection

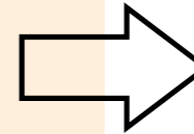
## PMT

high gain  
good timing  
not MR compatible



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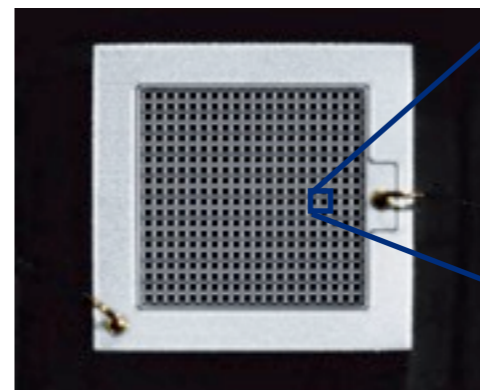


## SiPM (Silicon PhotoMultipliers)

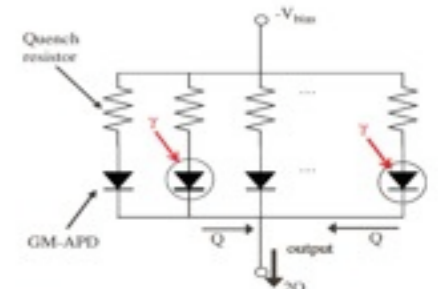
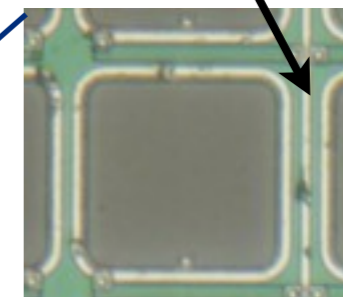
**SiPM** is the dominating technique for  
**all new PET developments**

### :-) ...Advantages :

- insensitive to magnetic field
- compact
- gain ~ PMT => excellent timing resolution + no need of very special care in the FE
- high PDE
- low bias voltage
- exist in arrays of increasing dimensions



single APD cell operated in Geiger mode



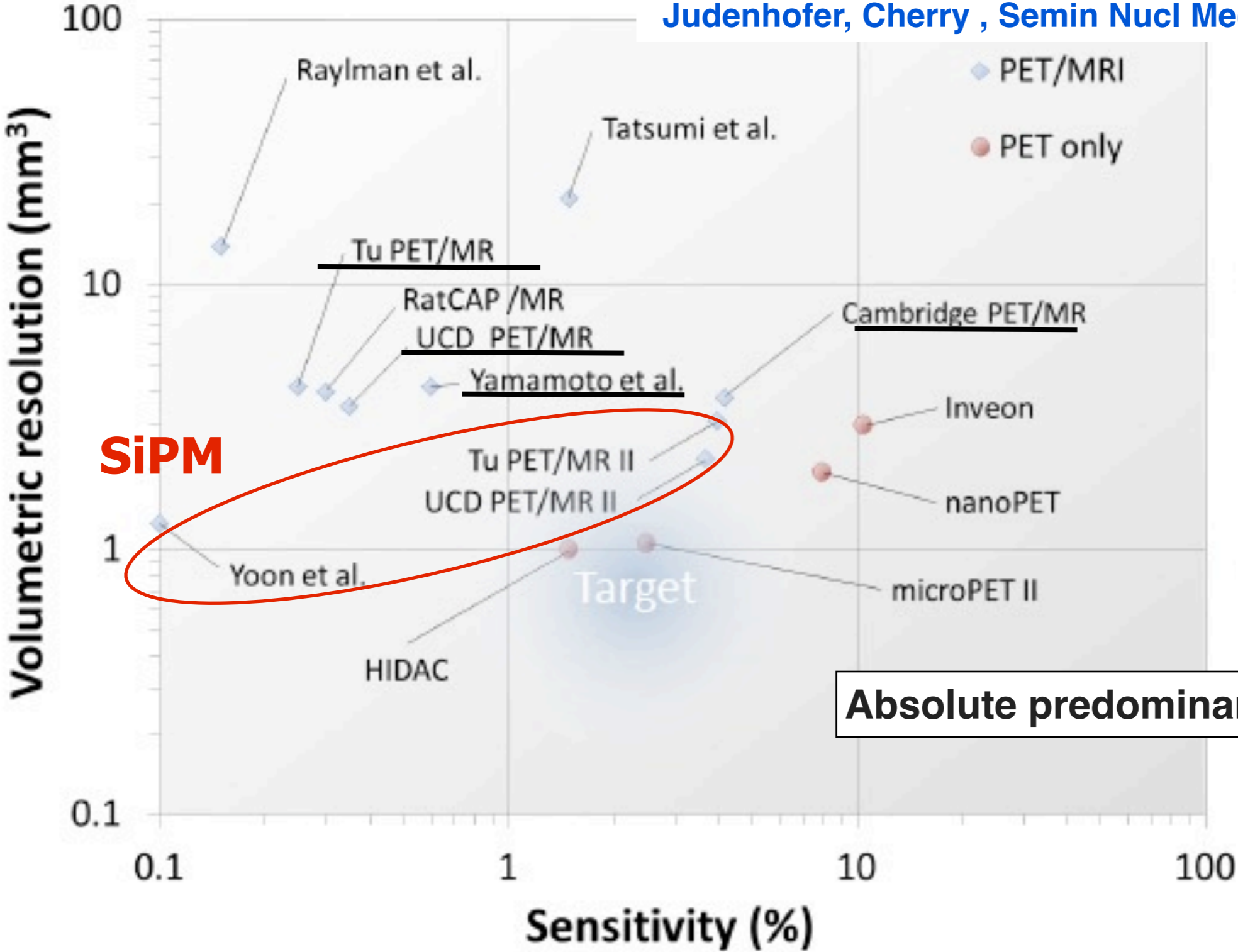
nr cells ~ 100 to 15000 / mm<sup>2</sup>  
typical cell size ~ 20 to 100 μm

### :-( ...Disadvantages

- temperature dependence of the gain => stability issues (Temp, Vbias) / cooling (- dark counts)
- non - linearity

# Overview of current small animal PET and PET/MRI

Judenhofer, Cherry, Semin Nucl Med 2013; 43(1):19-29



**SiPM**

**Absolute predominance of PET/MRI**

**Trend : improve sensitivity and spatial resolution**



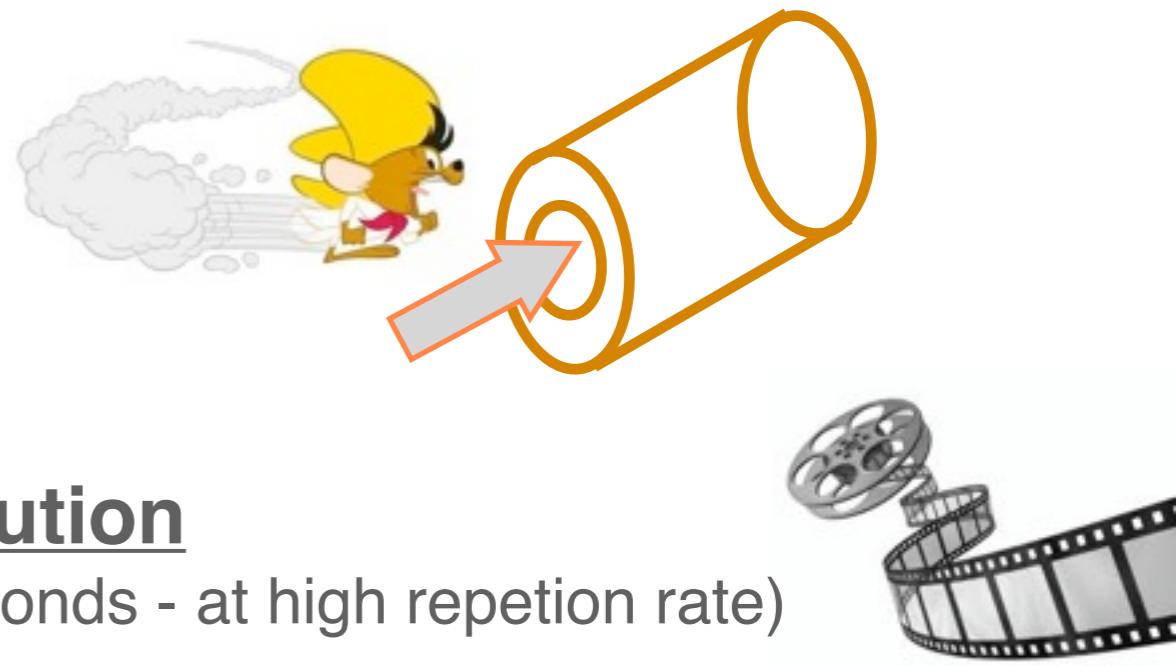
S  FIR

# SAFIR : GOAL

## Small Animal Fast Insert for mRi :

- pre-clinical PET / MRI
- fully simultaneous
- unprecedented high temporal resolution  
(acquisition duration of the order of a few seconds - at high repetition rate)
- dynamic studies of various biological processes  
(e.g. blood perfusion - cerebral blood flow with O-15)

<sup>15</sup>O : t1/2 ~ 2 mins ; changes in tracer concentration ~ 20% in secs



ETH / UniZh IBT (Institute of Biomedical Engineering)

- target user of the detector

ETH IPP (Institute for Particle Physics)

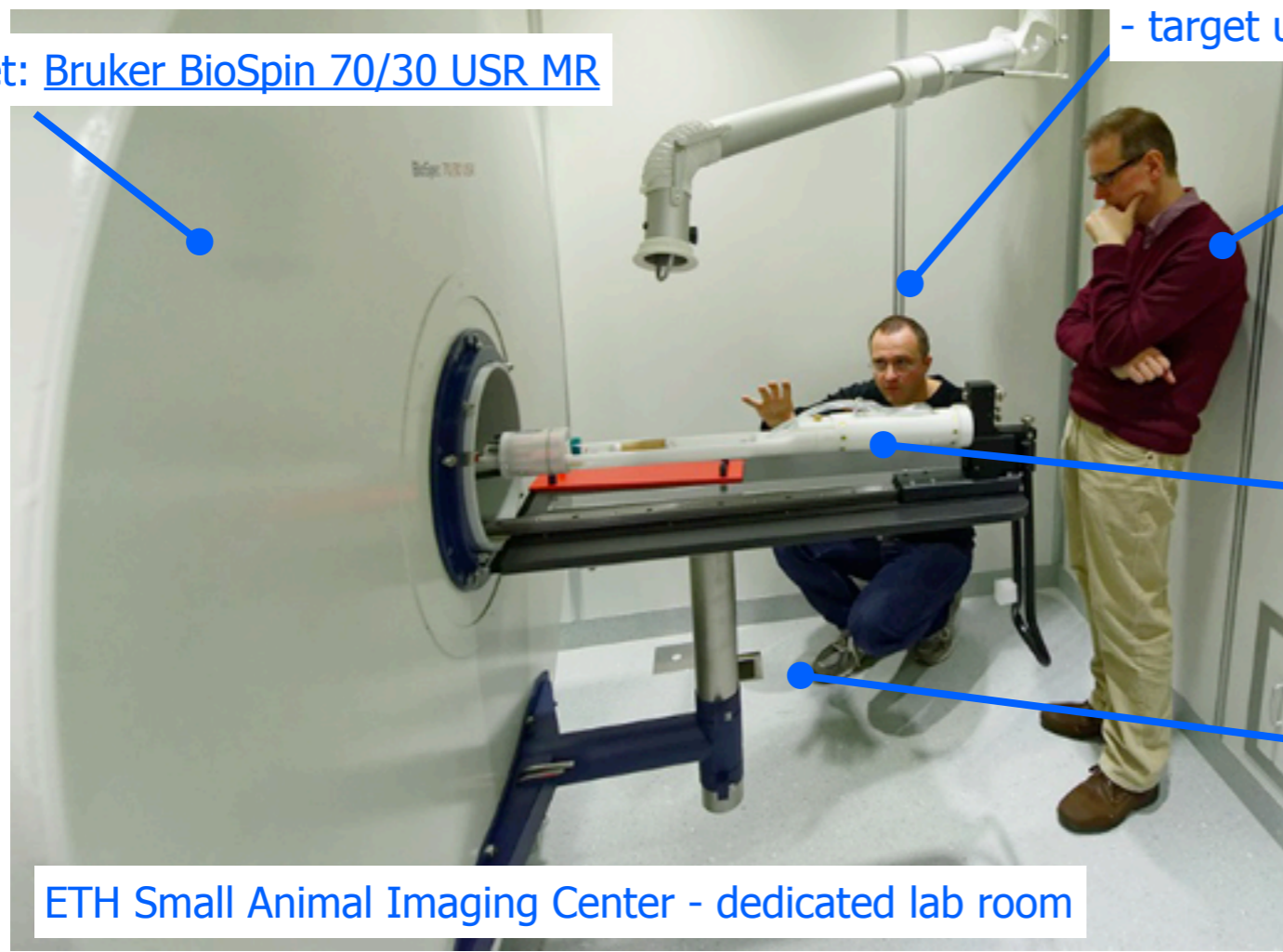
- detector conception, construction, commissioning...

Magnet: Bruker BioSpin 70/30 USR MR

space for the insert

direct tubing connection to the cyclotron hall (mainly for 15-O)

ETH Small Animal Imaging Center - dedicated lab room



# Detector requirements

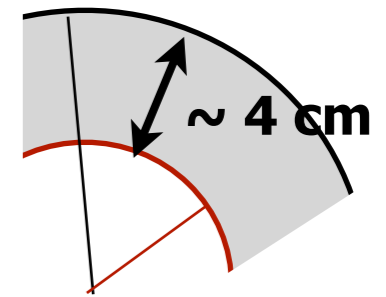
Challenging detector requirements => DETECTOR DESIGN

- Geometrical constraints
- Good spatial resolution
- **MRI- compatibility**

$\varnothing$ inner ~ 120 mm -  $\varnothing$ outer = 200 mm

R ~ 2 mm FWHM

limitations from the existing magnet

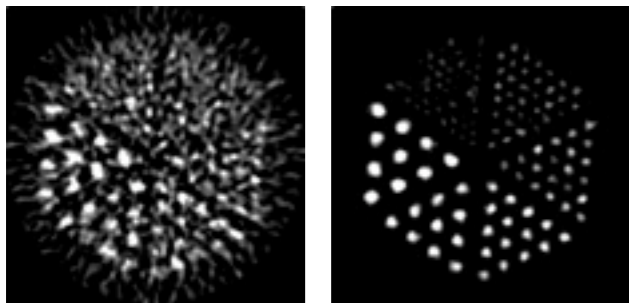


- Dynamic acquisition, **few seconds temporal resolution**

=> poor statistics - poor image quality

50 kcounts

500 kcounts



**high sensitivity: S ~ 5%** (at photopeak)

high injected activities

**up to ~ 500 MBq** [standard pre-clinical ~ 50 MBq]

Randoms contribution!

readout and DAQ system

small coincidence window (<ns)

min. deadtime and pileup

**excellent coinc. time resolution CRT ~ 300 ps FWHM**

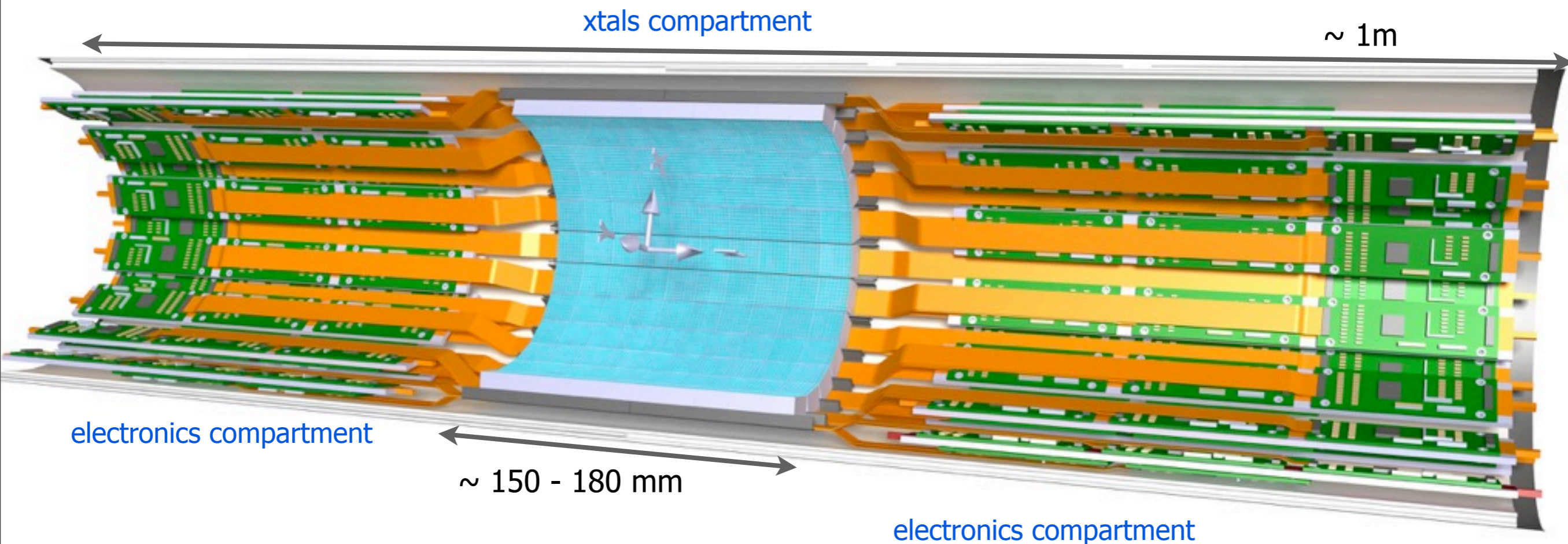
[same as in clinical TOF-PET, without being TOF-PET!]

1:1 coupling xtal/SiPM  
**high channel number**  
**high channel density**

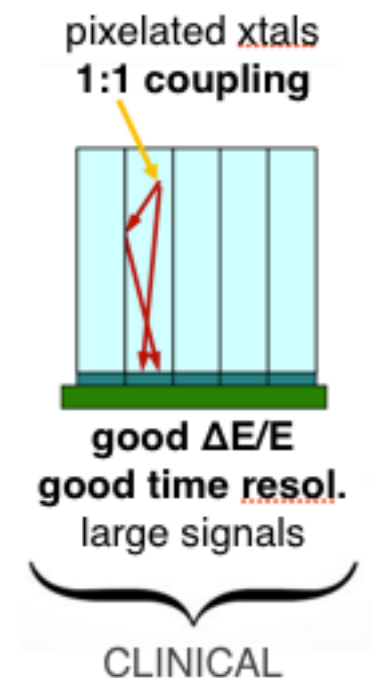
high rate/channel  
**~ 10 kHz/mm<sup>2</sup>**

# SAFIR design concept

sketch of 1/2 detector  
design not yet finalized!



- radial arrangement of crystal matrices with 1:1 coupling to SiPM arrays
- LSO-type (LYSO, LSO:Ca...) crystal matrices
- modular structure of crystals
- ring structure / several modules per ring
- rings stacked axially to provide the axial FOV coverage



# Mechanics for the insert

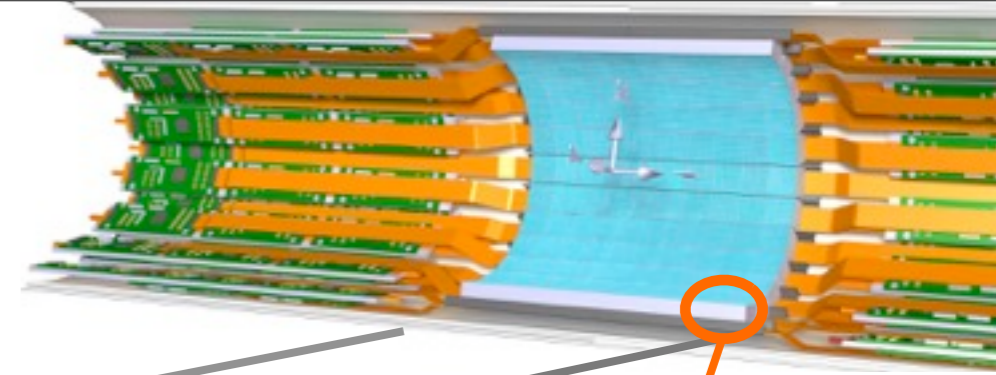
- mechanical support
- RF shielding

polycarbonate coverage

fiberglass composite

thermal insulation btw xtals+SiPM and animal

inflatable seals

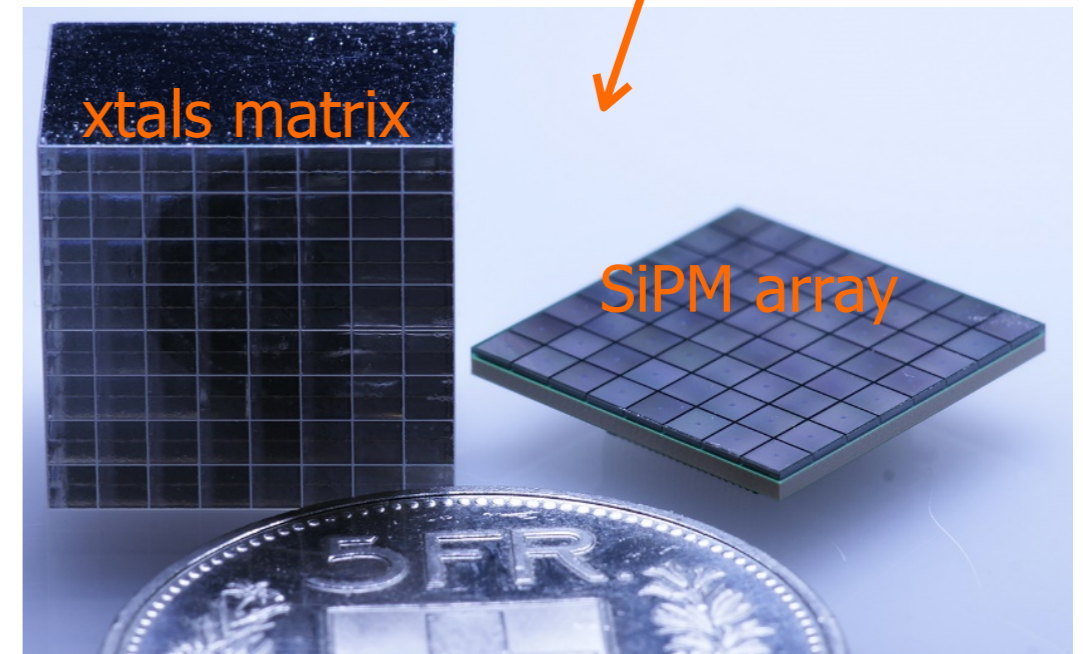


## Reference design

- not necessarily the final design
- one possible configuration for the detector based on commercially available components

- xtals :  $(2.1 \times 2.1 \times 12) \text{ mm}^3$  , 2.2 mm pitch
- matrices 8x8
- 24 modules / ring
- 10 rings (axially stacked) : FOVax ~ 180mm
- Inner radius ~ 60 mm
- 15360 readout channels

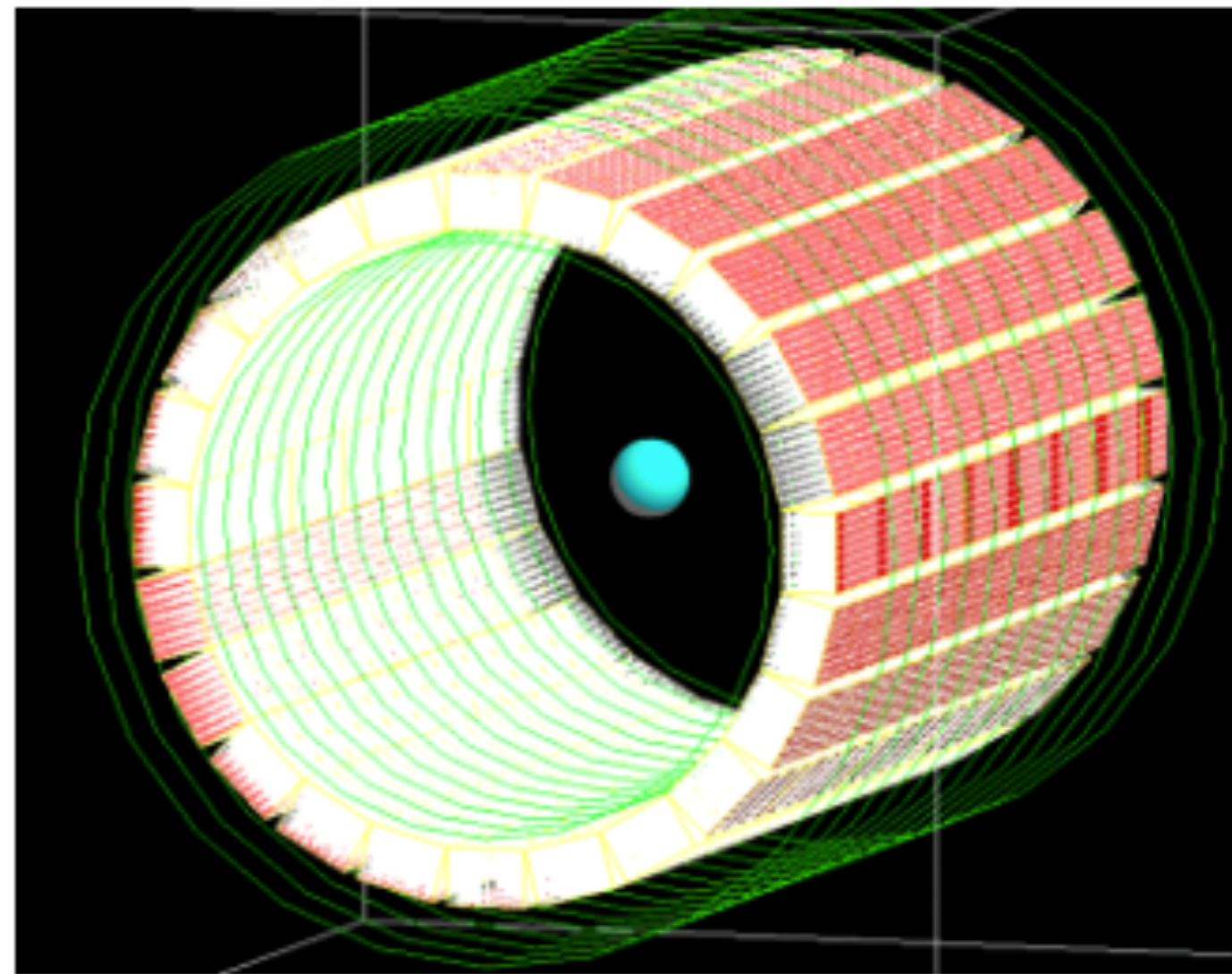
Reference design : needed for simulations



- 8x8 matrices
- pitch = 2.2 mm

# SAFIR SIMULATIONS

- custom simulation framework
- native **Geant4**
- DETECTOR
  - ‘reference’ design geometry
  - gaussian time smearing  
 $\sigma = 90 \text{ ps} \Rightarrow \text{CRT} \sim 300 \text{ ps fwhm}$
  - gaussian energy blurring  
 $\Delta E/E \sim 20\% \text{ fwhm}$



- according to  
[NEMA standard \(NU 4-2008\)](#) :
1. **Noise Equivalent Count Rate (NECR)**
  2. **Sensitivity**
  3. **Spatial resolution**

**NEMA (National Electrical Manufacturer Association):** standardized methodology to evaluate the performance of a scanner independently on the specificity of the designs.

sources and phantoms used in simulations according to NEMA prescriptions

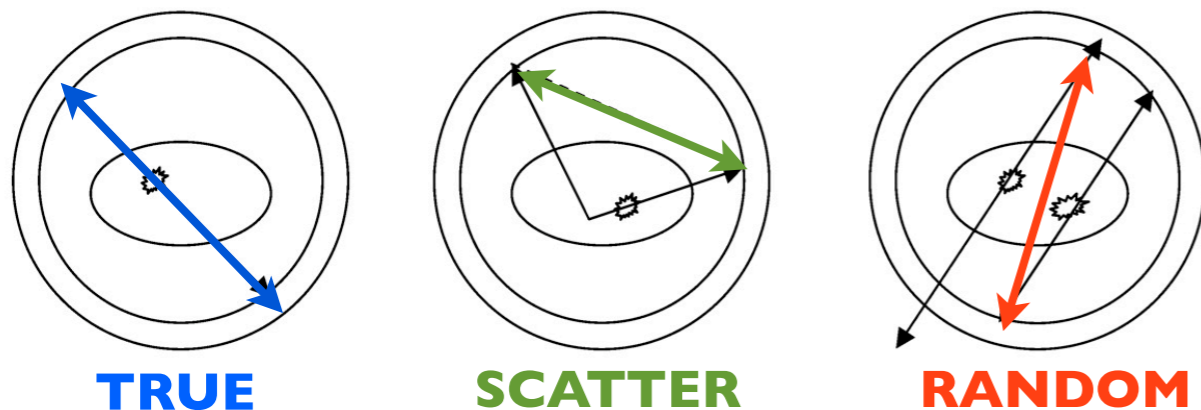
Quantity	Phantom Material	Phantom Shape	Source	Activity (MBq)
NECR	High-density polyethylene	Mouse-like (cylinder, l=70 mm, d=25 mm)	$^{18}\text{F}$ line (l=60 mm)	10, 25, 50, 100, 200, 300, 400, 500, 700, 1000
Sensitivity	Acryl	Cube (1 cm x 1 cm x 1 cm)	$^{22}\text{Na}$ point-like	0.1
Spatial resolution	Acryl	Cube (1 cm x 1 cm x 1 cm)	$^{22}\text{Na}$ point-like	0.1



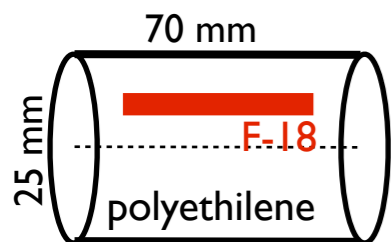
# NECR (Noise Equivalent Count Rate)

- figure of merit in PET (counting statistics)
- NECR = rate of 'true' coincidences normalized to the total number of coincidences

$$\text{NECR} = T^2 / (T+S+R)$$

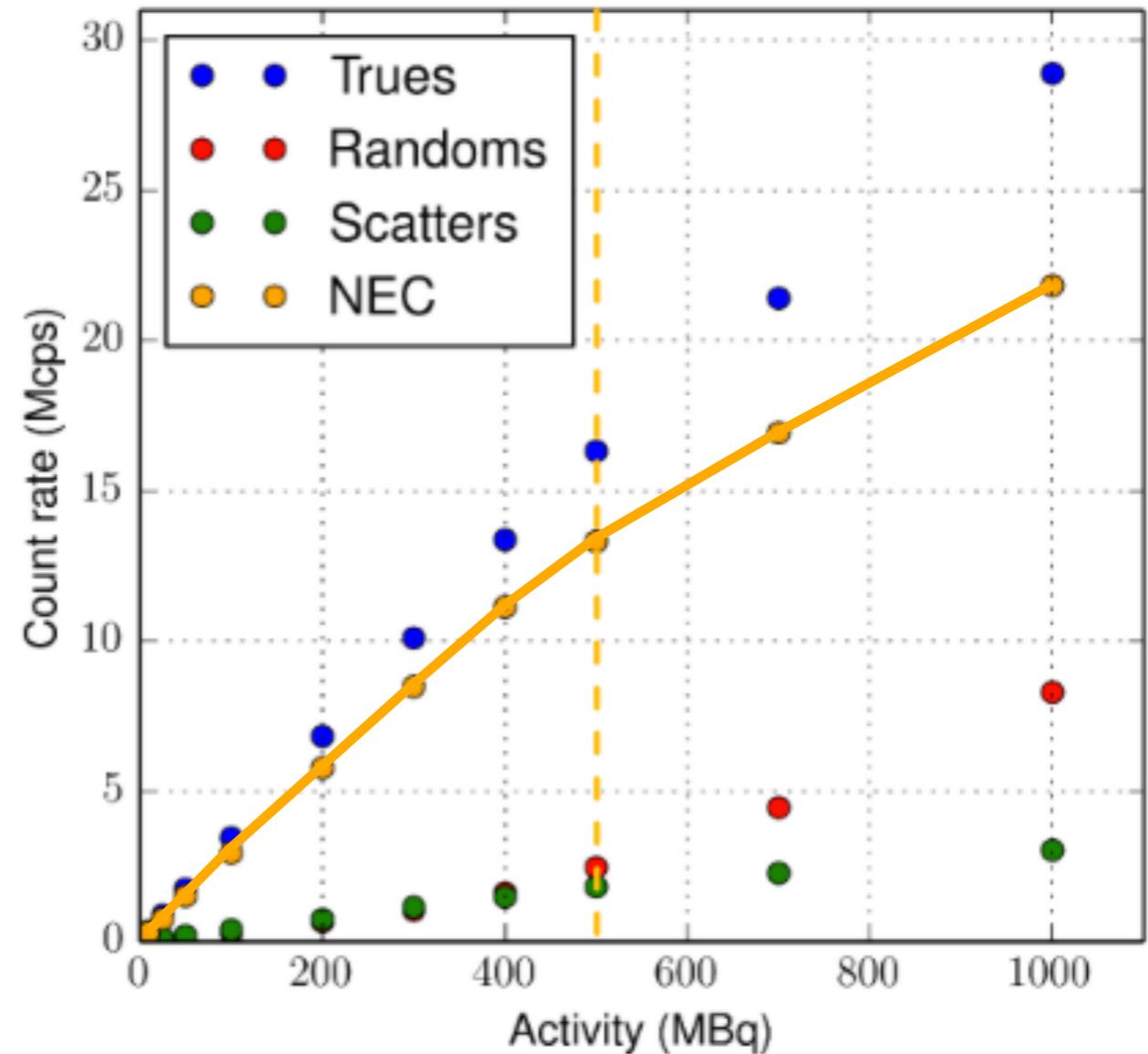


NEMA prescriptions :



mouse cylindrical phantom with line source at different activities

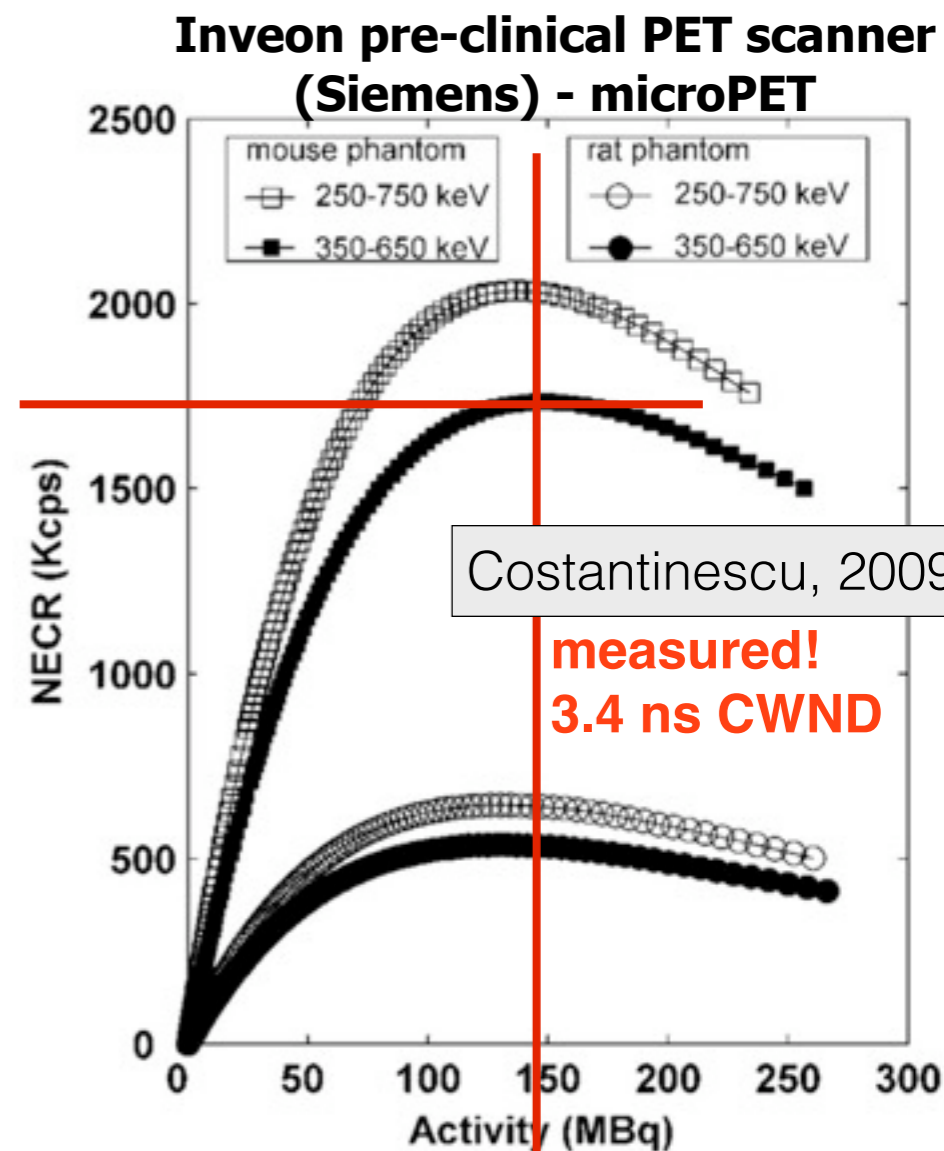
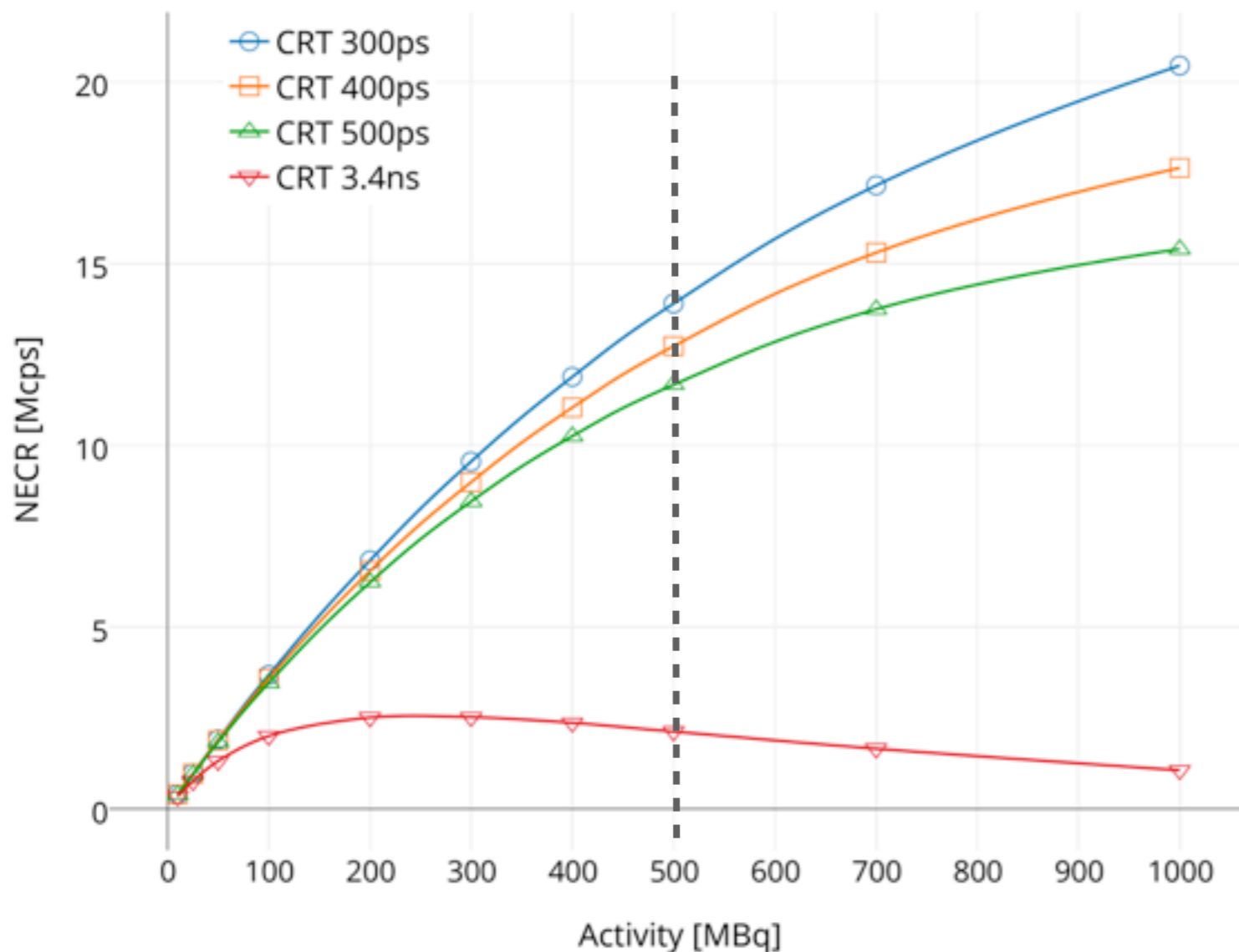
from simulated data  
(with reference design geometry)



- higher **NECR value** => higher ratio of good events (T) to the overall detected events (T, R, S) i.e. S/N
- larger activity **peak value** => capability to handle higher activities without being dominated by the randoms + scatters

# NECR (Noise Equivalent Count Rate) vs CRT

strong impact of the timing resolution on the NECR



## ⇒ Feasibility of the SAFIR concept

with CRT ~ a few 100's ps (<500 ps) and at Act ~ 500 MBq

(1) still far from being dominated by randoms

(2) NECR ~ x6/7 'standard NECR' at activities (~ 50 MBq) (i.e. 1 min ⇒ 10 secs)

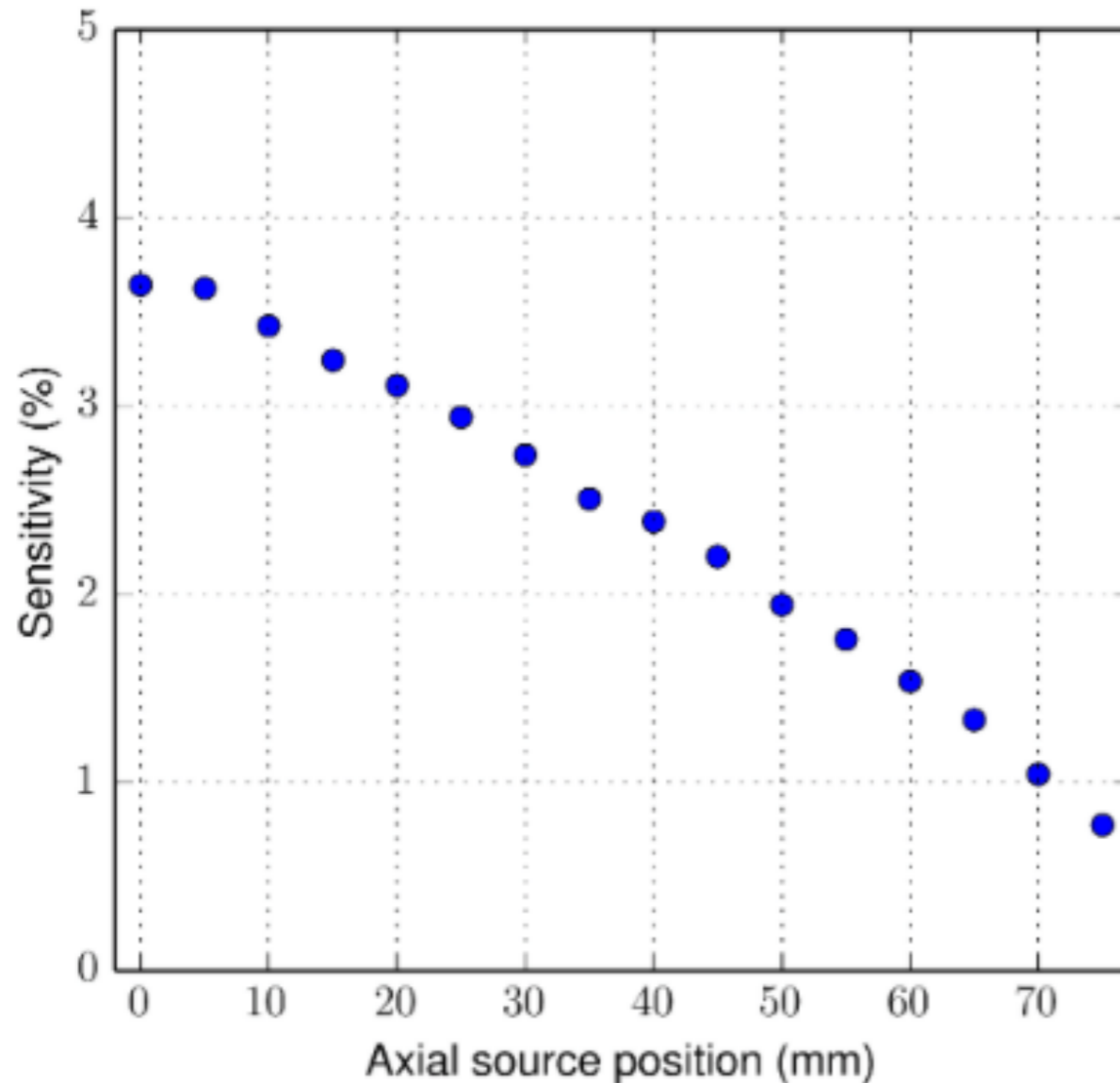
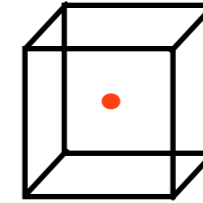
# Sensitivity

from simulated data  
(with reference design geometry)

**Sensitivity** =  $N_{\text{detected\_coincs}} / N_{\text{annihilations}}$  - at photopeak

$N_{\text{detected\_coincs}}$  &  $N_{\text{annihilations}}$  defined according to NEMA standard

- NEMA phantom : 1cm<sup>3</sup> acrylic with <sup>22</sup>Na point source at the center
- low activity (Act = 100 kBq)
- at different axial distances

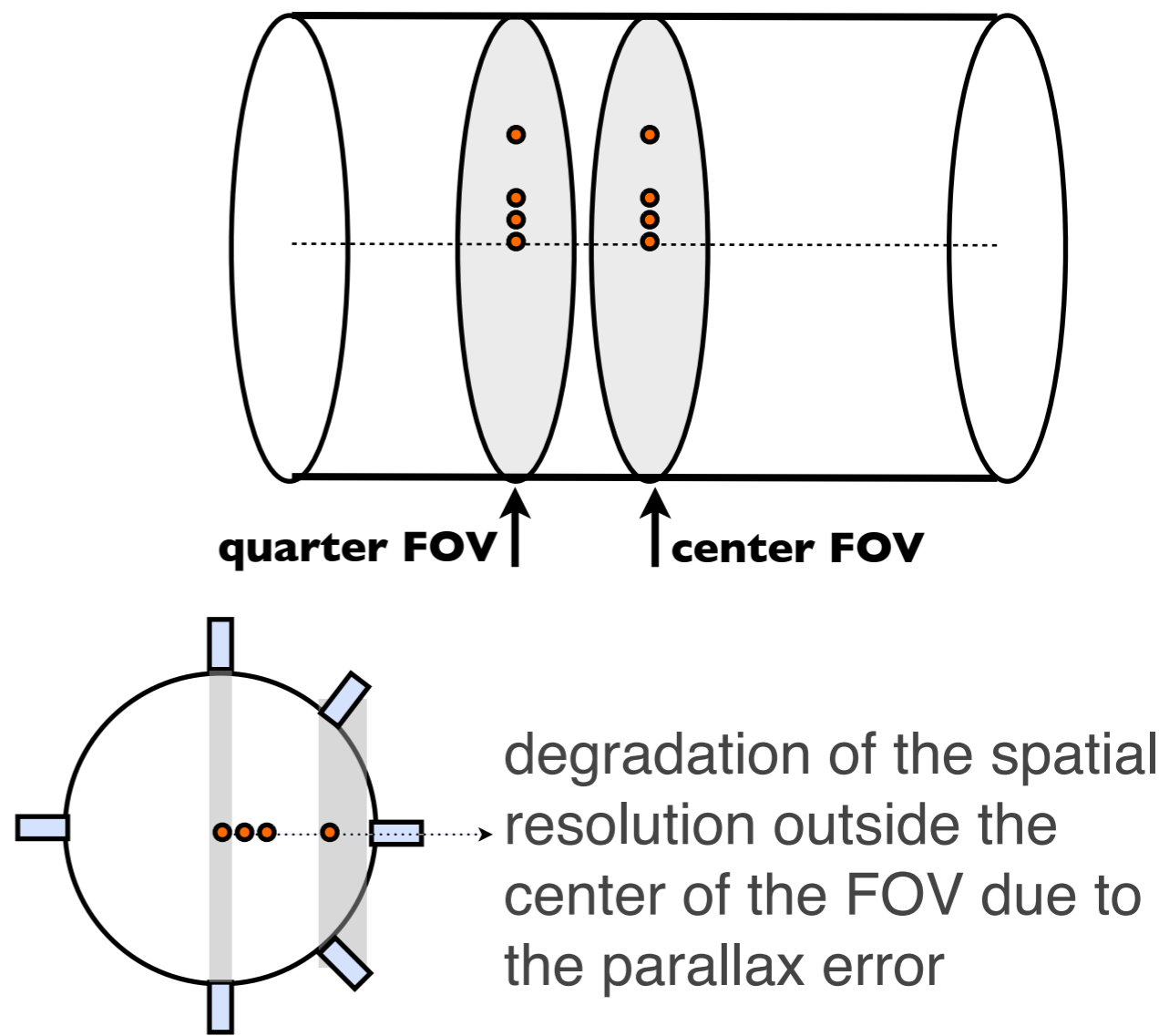
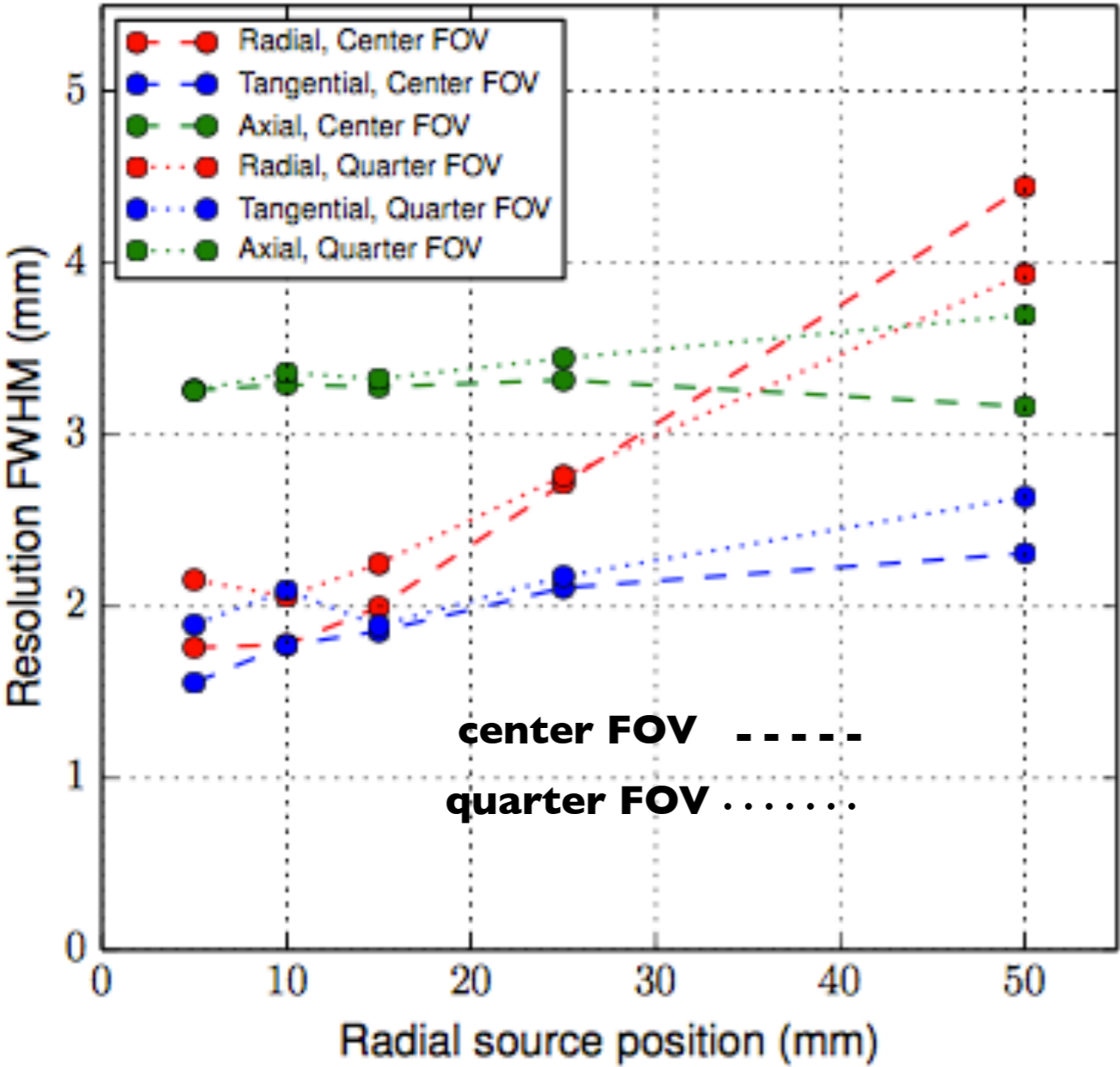


**S<sub>peak</sub> ~ 3.8%** (at photopeak)

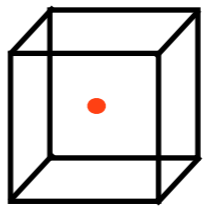
- Large solid angle coverage (~ 85%) => **Very good sensitivity**
- expected to increase with the inclusion of ICS (Inter-Crystal Scattering) events

# Spatial resolution

from simulated data  
(with reference design geometry)



- NEMA phantom : 1cm<sup>3</sup> acrylic with 22-Na point source at the center
- low activity (Act = 100 kBq)
- at different radial distances in two different axial positions



**Resolution ~ 2mm FWHM (at center of FOV)**

# SAFIR image reconstruction

## STIR (Software for Tomographic Image Reconstruction)

- Open Source software (C++)
- libraries for image reconstruction and manipulation of projection data
- several reconstruction algorithms already implemented

### Goal :

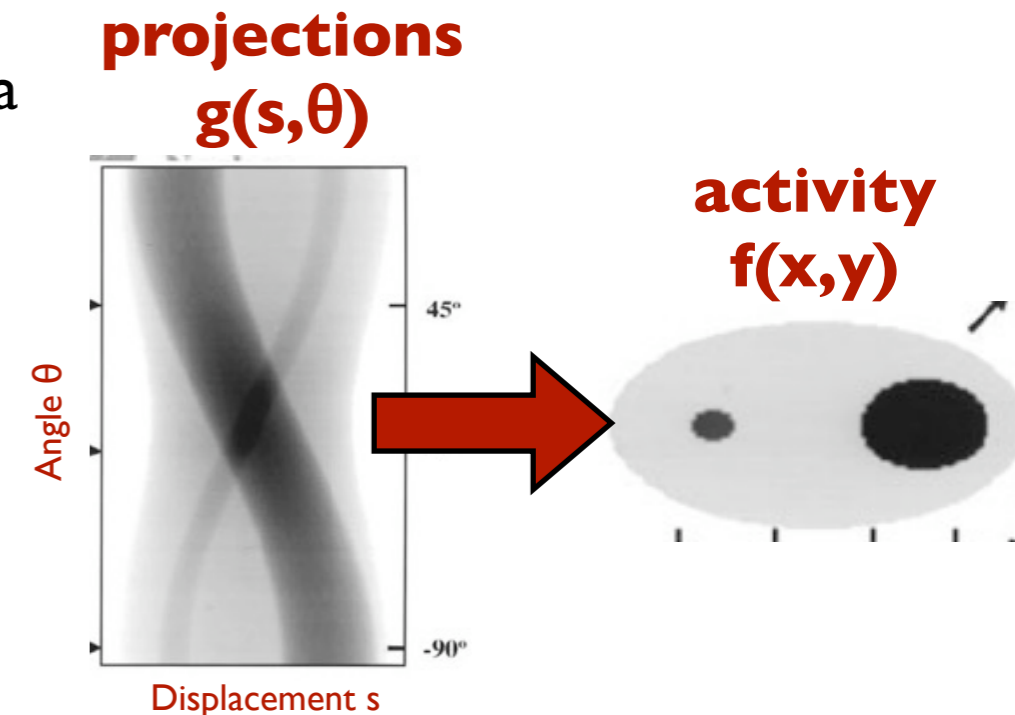
recover the activity distribution, starting from the acquired data

### Data :

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

**$f(x,y) \Rightarrow g(s,\theta)$  : data taking (projection)**

**$g(s,\theta) \Rightarrow f(x,y)$  : back projection**



Two different approaches :

### ANALYTICAL METHOD

- Filtered Back Projection (FBP) :
  - 1) Fourier analysis of the projection data
  - 2) Different weight to different frequencies (“filtering”)
  - 3) “Back-Project”
- **simple and fast / less accurate**

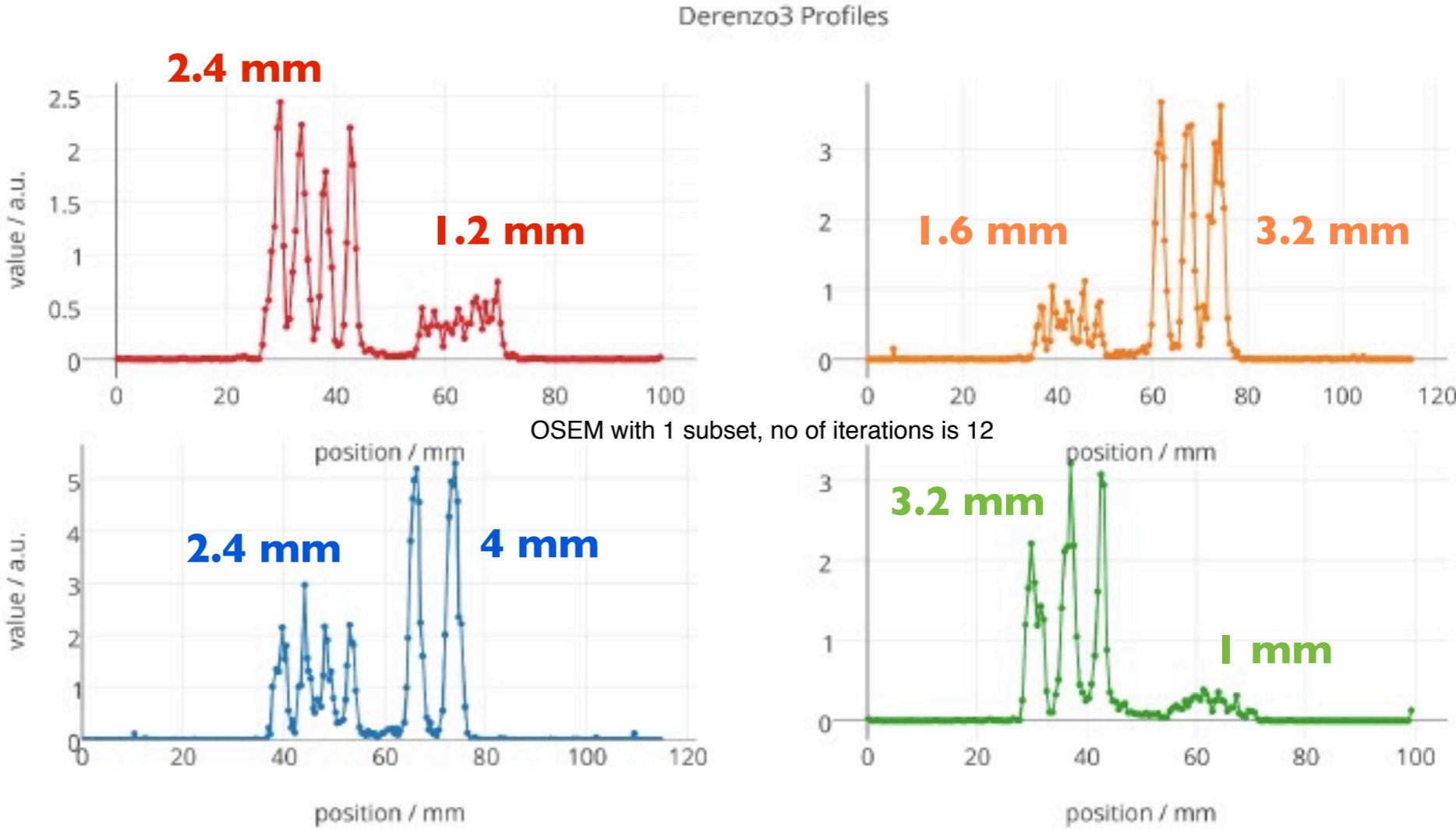
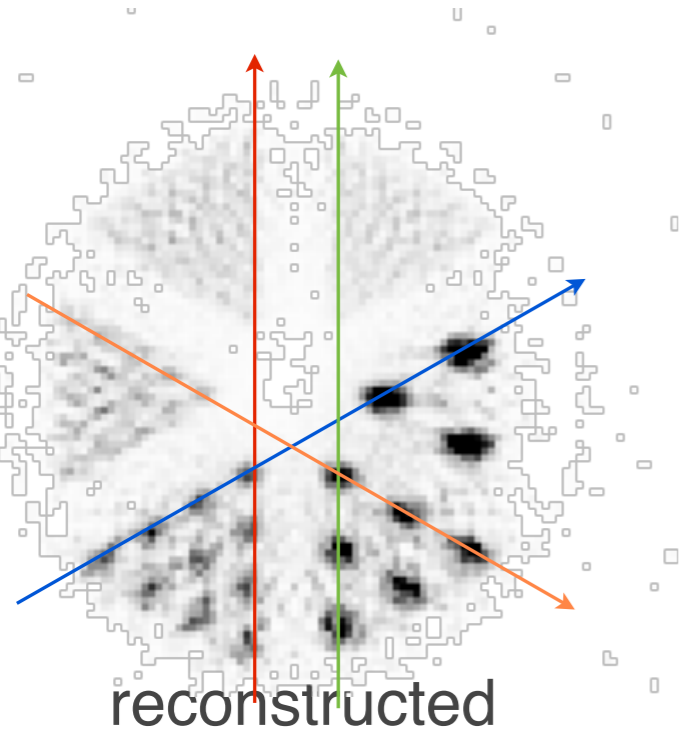
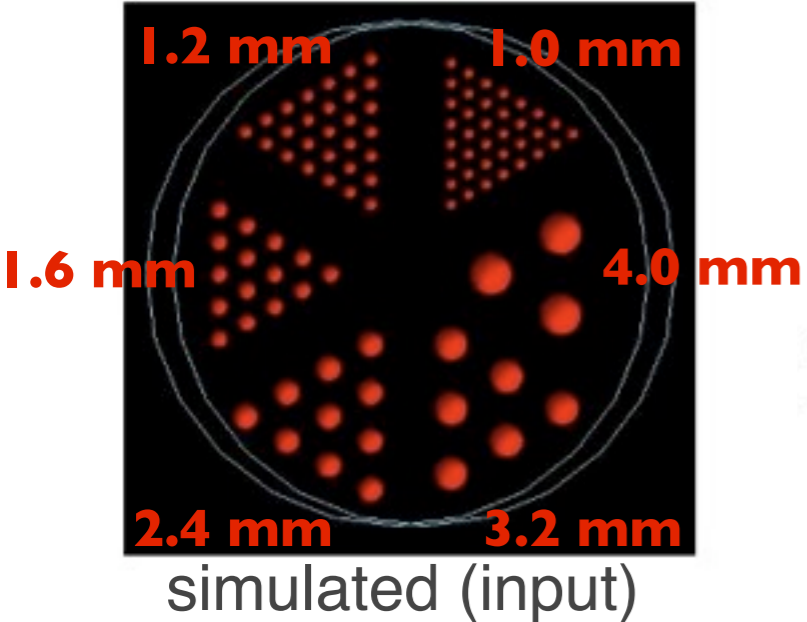
### ITERATIVE METHOD

- optimization procedure until the best estimate of the source is found (several optimization strategies exist)
- it requires the accurate model of the emission and detection processes
- **slow and CPU consuming**
- **accurate reconstruction**

# SAFIR image reconstruction (static)

Derenzo phantom - no background

- iterative (OSEM - 1 subset - 12 iterations)
- 1 sec data
- 500 M decay events
- "best case scenario"

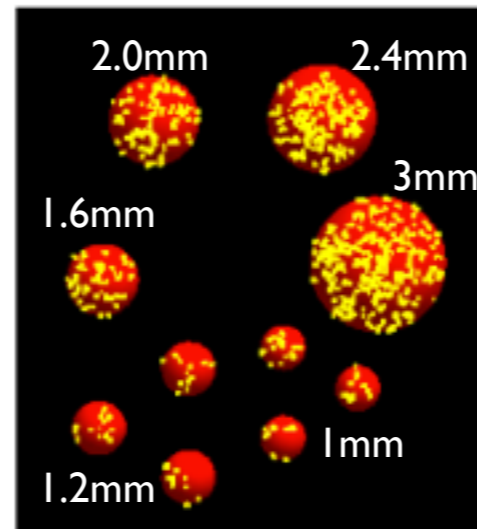
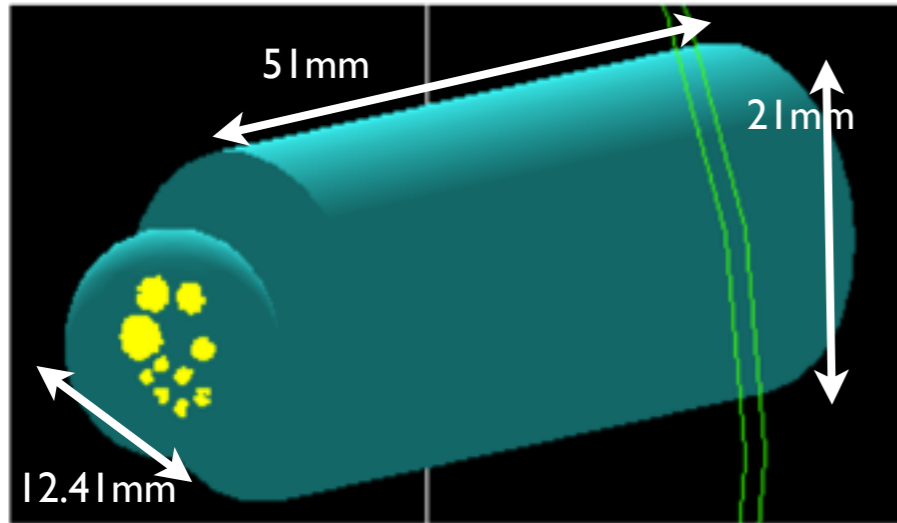


=> Image reconstruction :  
- up to 1.6 mm structures are ~ resolvable

# SAFIR image reconstruction - plans

## Currently ongoing activities :

- simplified mouse phantom with realistic activity concentrations

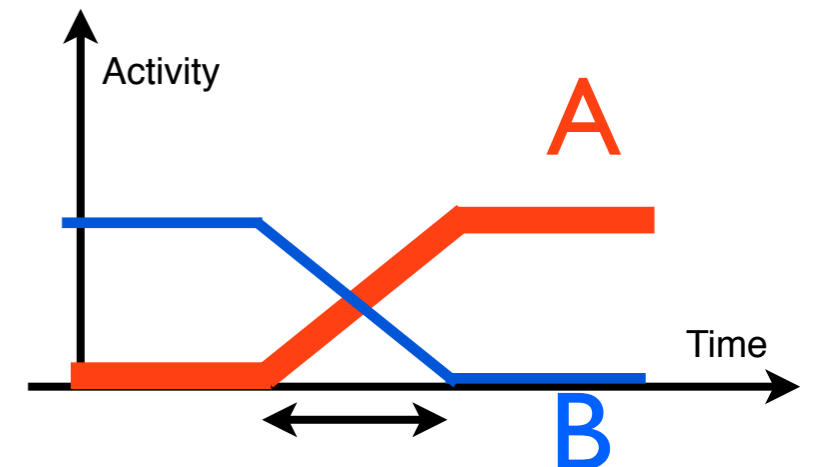
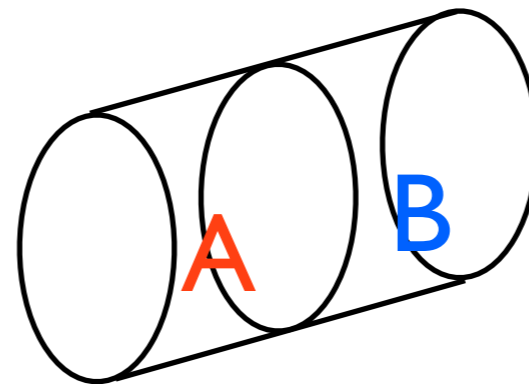


body / brain / spheres

- towards dynamic reconstruction

time slicing of the transient region

division of the full data set into a time sequence of data frames



- future : from frame-based reconstruction to 4D reconstruction algorithms

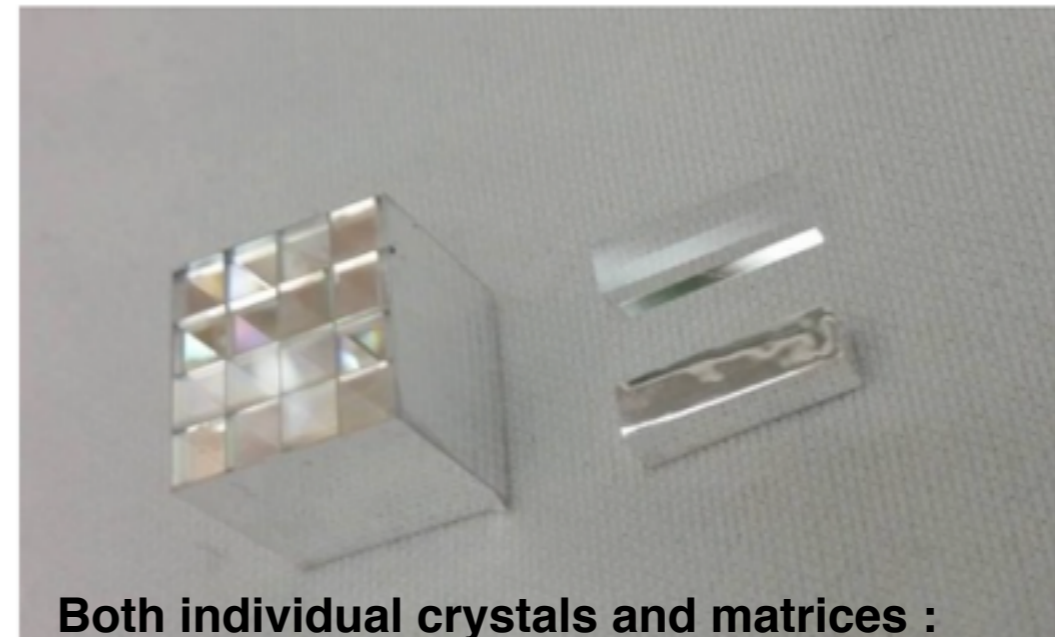
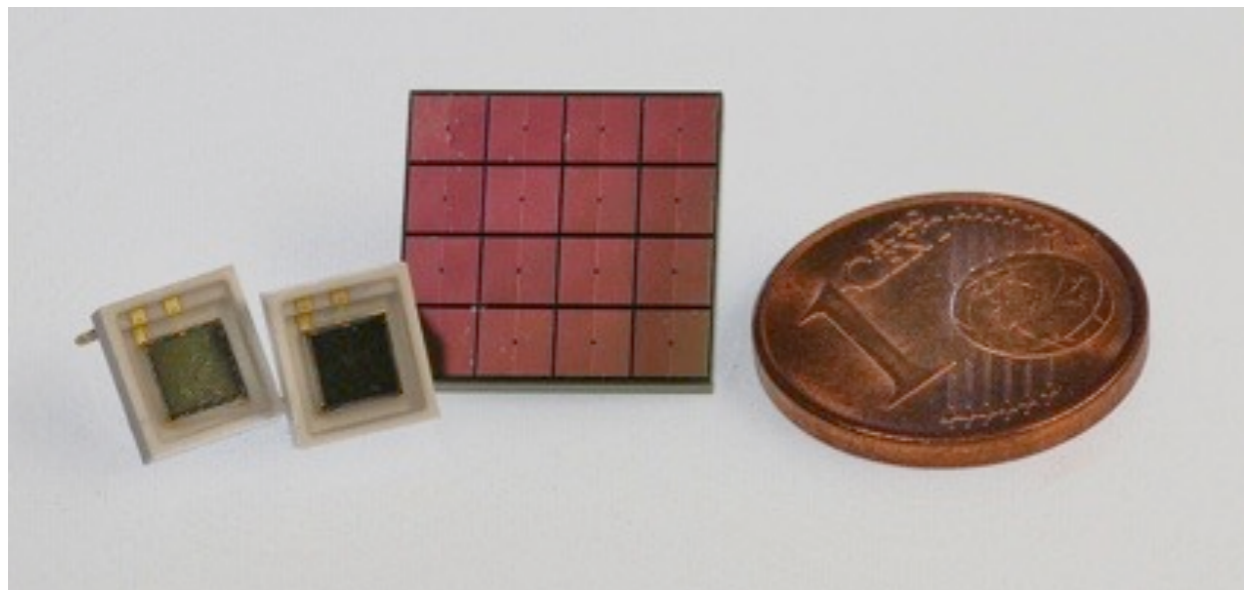
# Characterization of hardware components

Hardware components:

- **SiPMs**
- **crystals**
- **readout chips for SiPM**

A few samples of arrays in the 'reference' design (i.e. 8x8 arrays, pitch 2.2 mm) have been procured only recently

**Tests done so far** : on individual crystals / SiPM or 4x4 arrays (3.2 mm pitch)



Both individual crystals and matrices :

LYSO (Hilger)

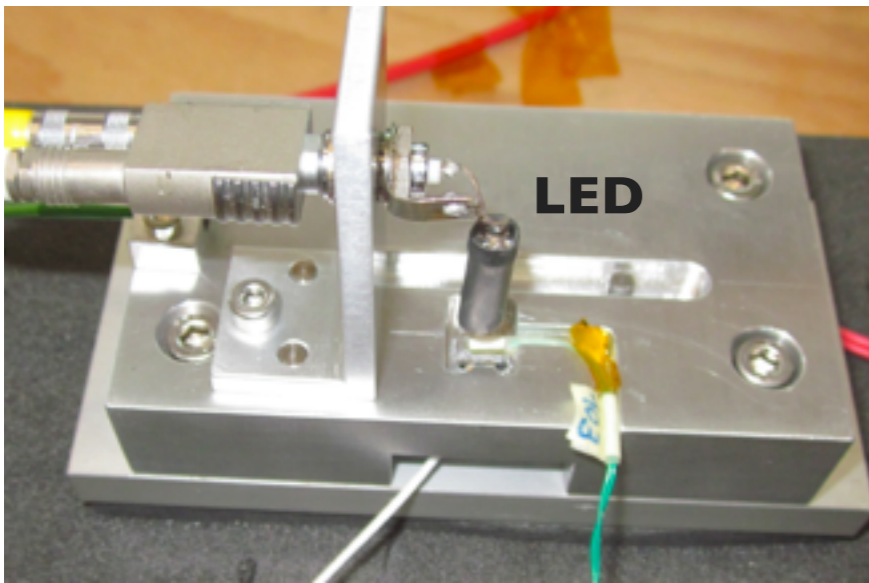
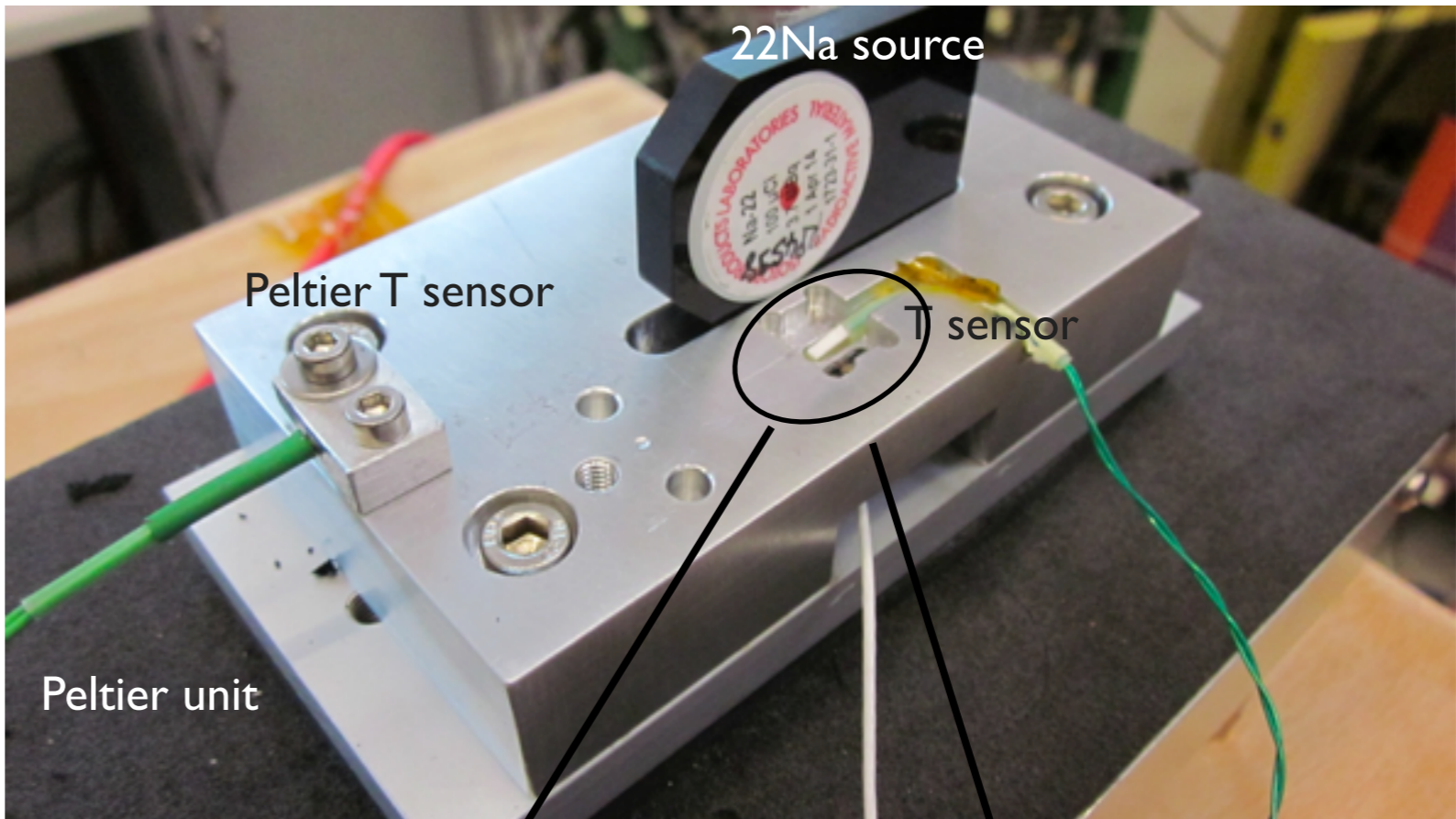
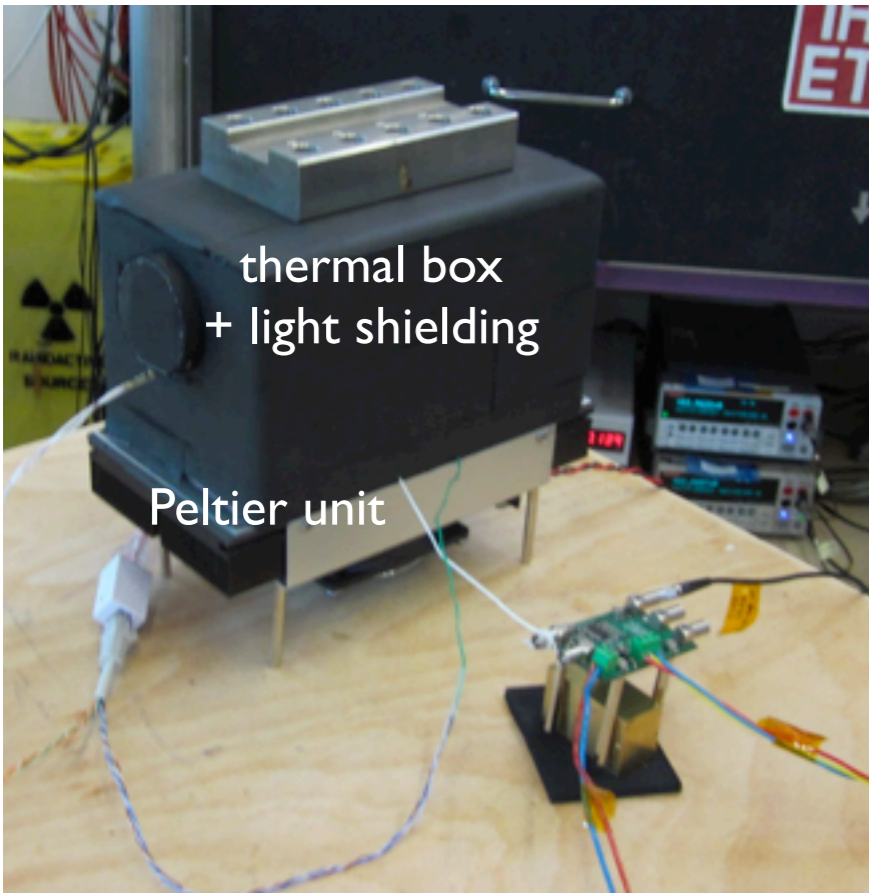
LYSO (Agile)

LFS (Hamamatsu)

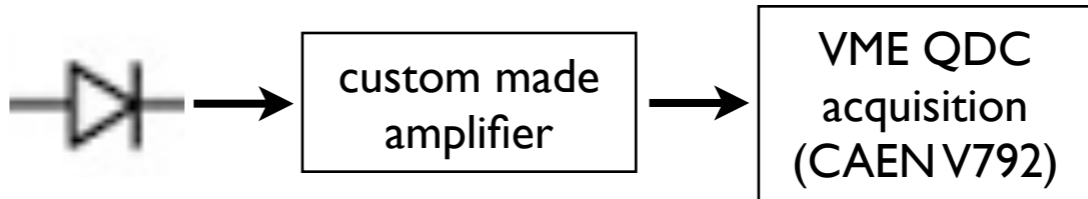
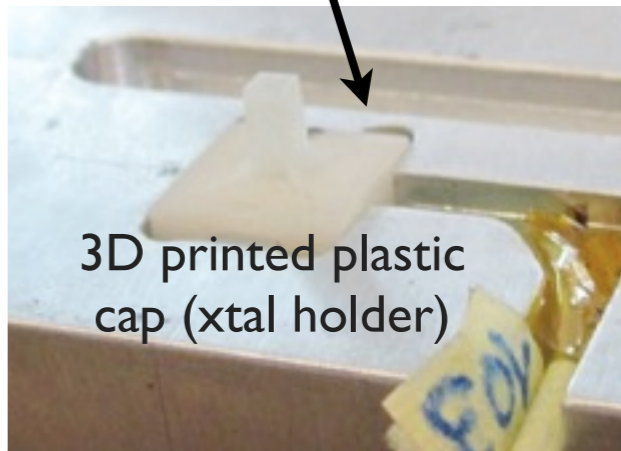
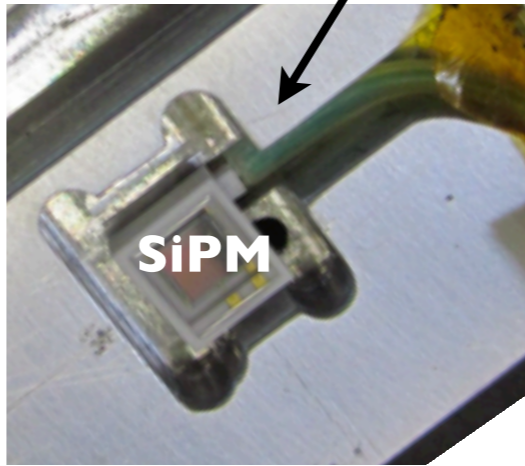
LSO & LSO:Ca (SiPAT) - only on single crystals



# Analogue characterization SiPM / crystals



same setup used with LED on bare SiPM for single photoelectrons detection



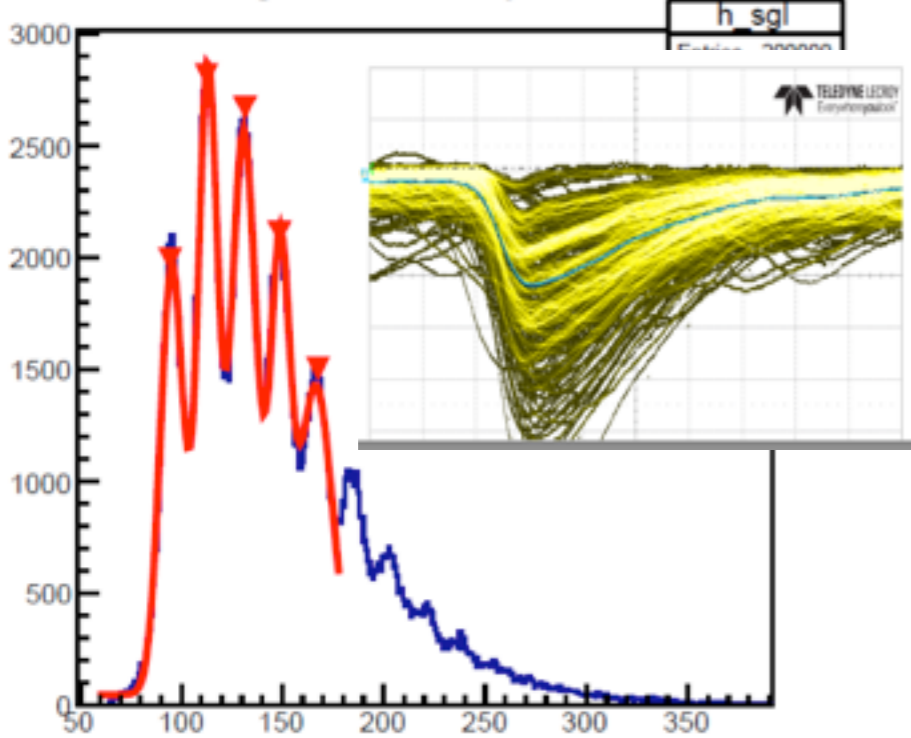
analogue readout chain

# Analogue characterization SiPM / crystals

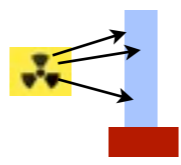
**LED (no crystal)**



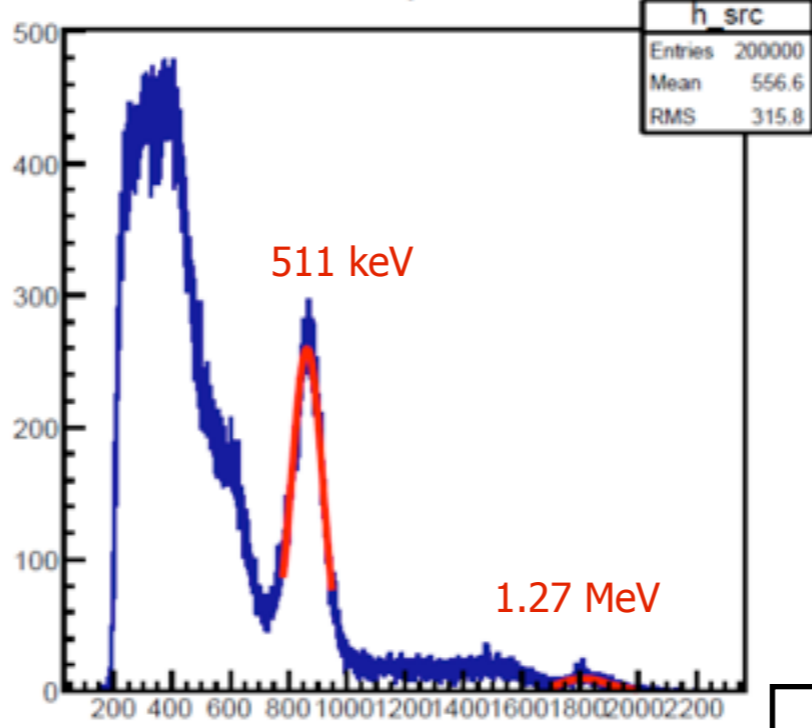
Single Photon Spectrum



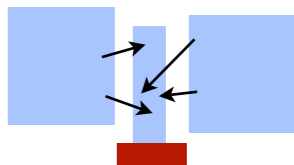
**$^{22}\text{Na}$  (with crystal)**



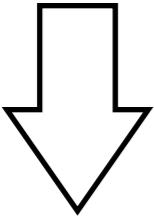
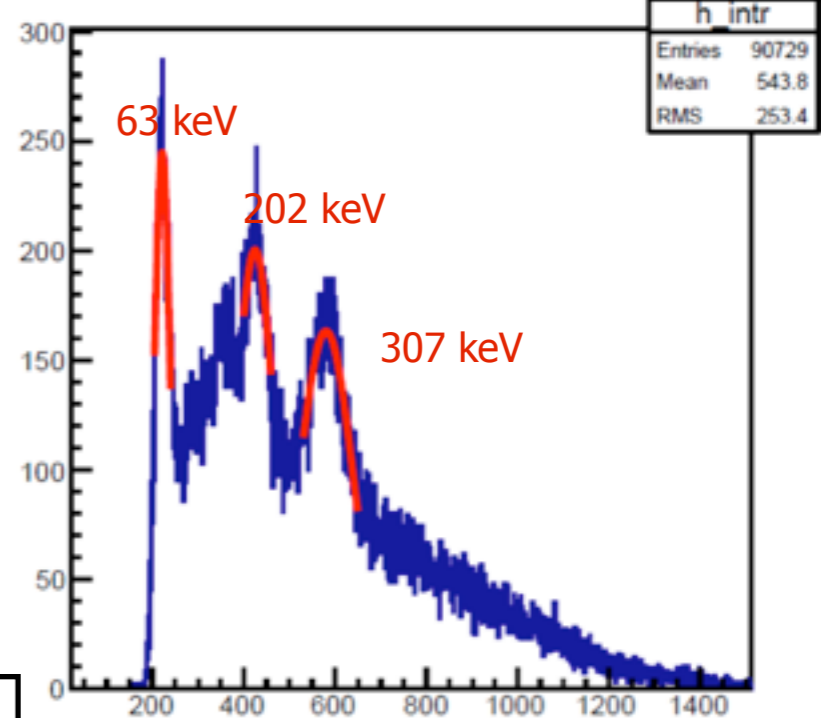
Na-22 Spectrum



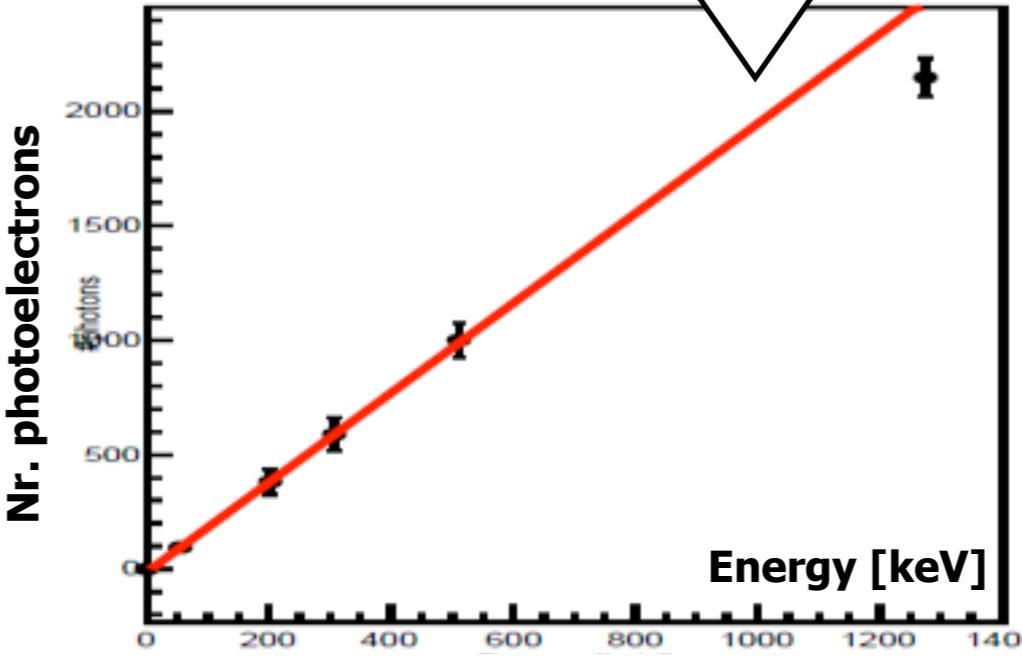
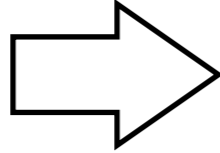
**external LYSO (with crystal)**



Intrinsic Radioactivity Spectrum



**Calibration**  
[ADC counts / pe]



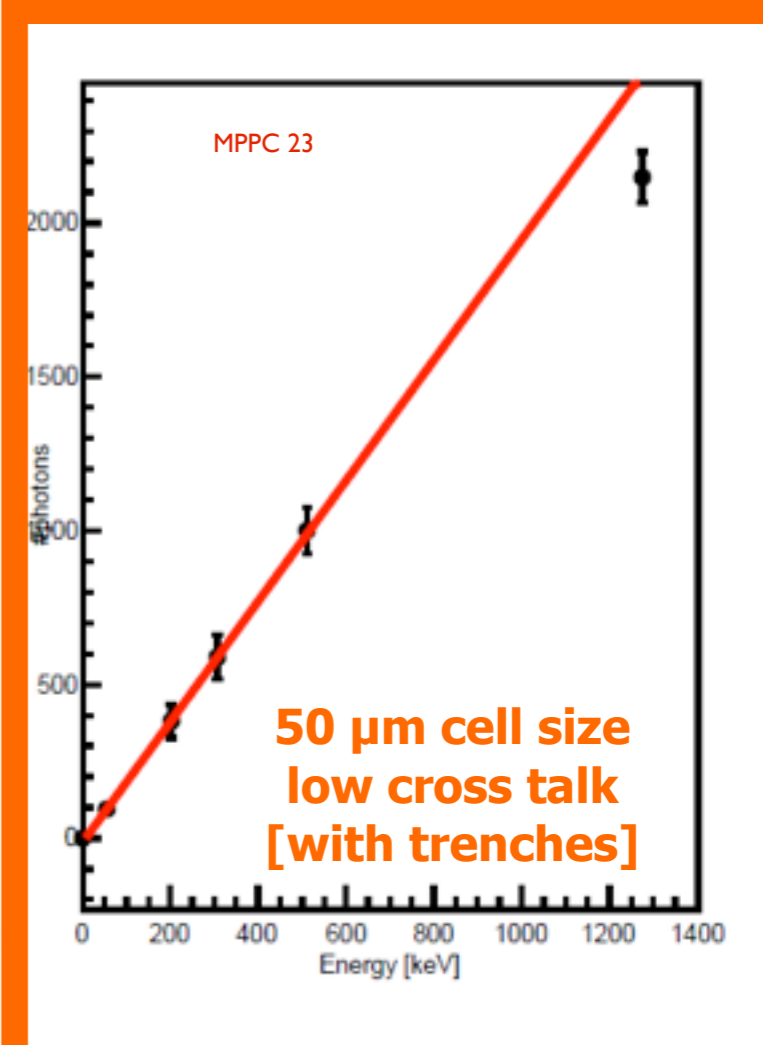
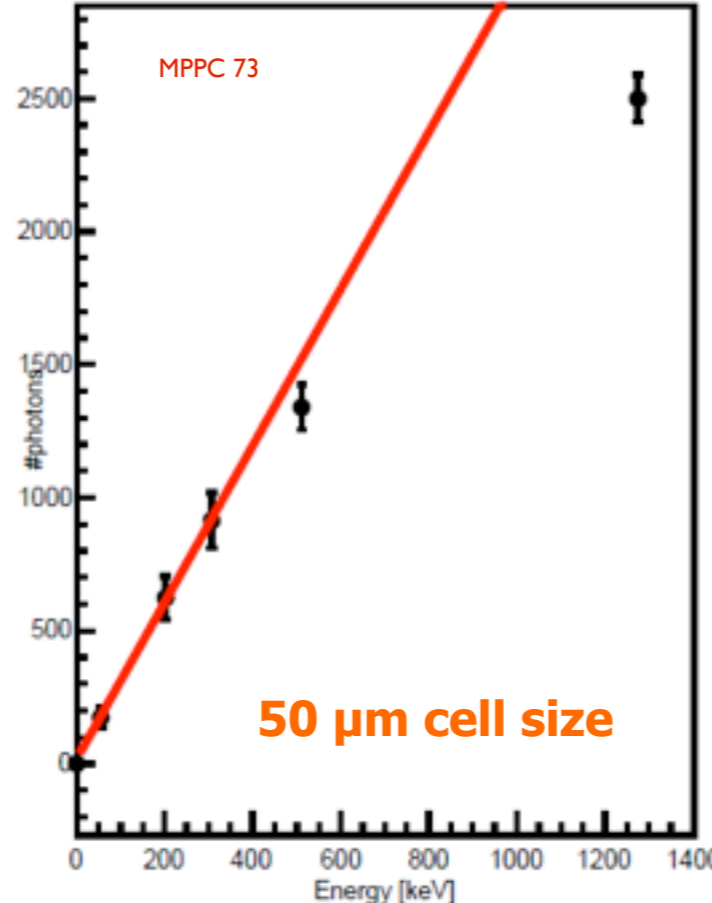
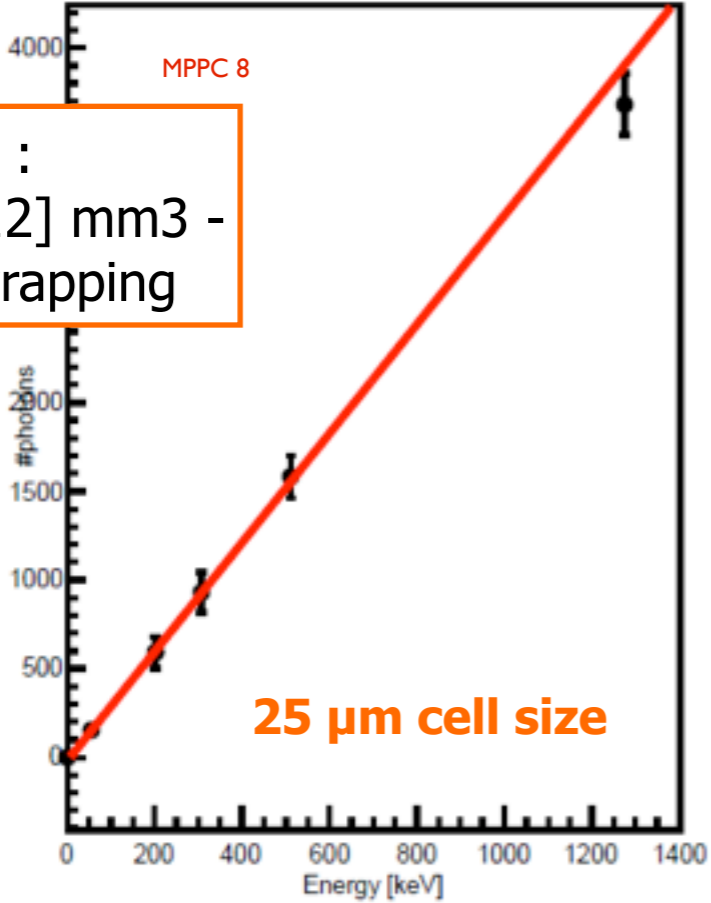
L(Y)SO crystals (1.5 x 1.5 x 12) mm<sup>3</sup>

# Analogue characterization SiPM / crystals

nr photoelectron vs energy

**XTAL :**  
[1.5 x 1.5 x 12] mm<sup>3</sup> -  
with ESR wrapping

**SiPM :**  
[3x3] mm<sup>2</sup>  
Hamamatsu



Light yield at the photopeak

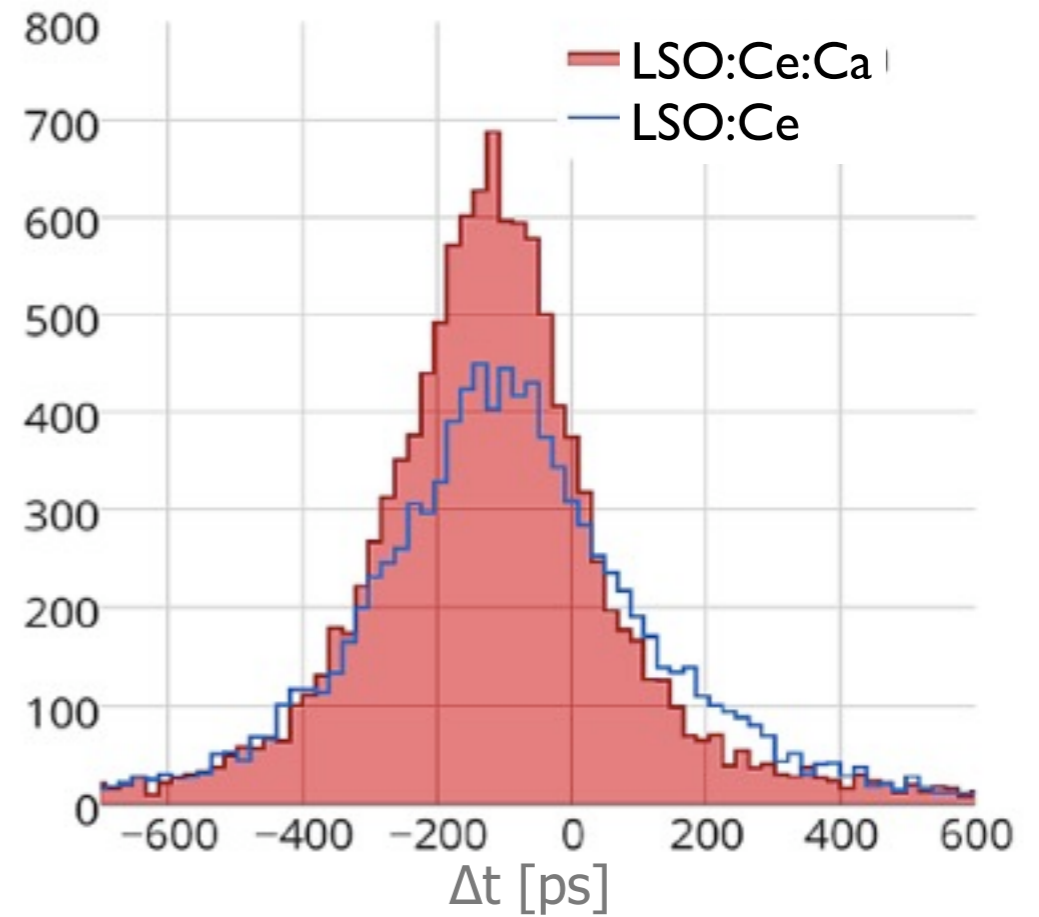
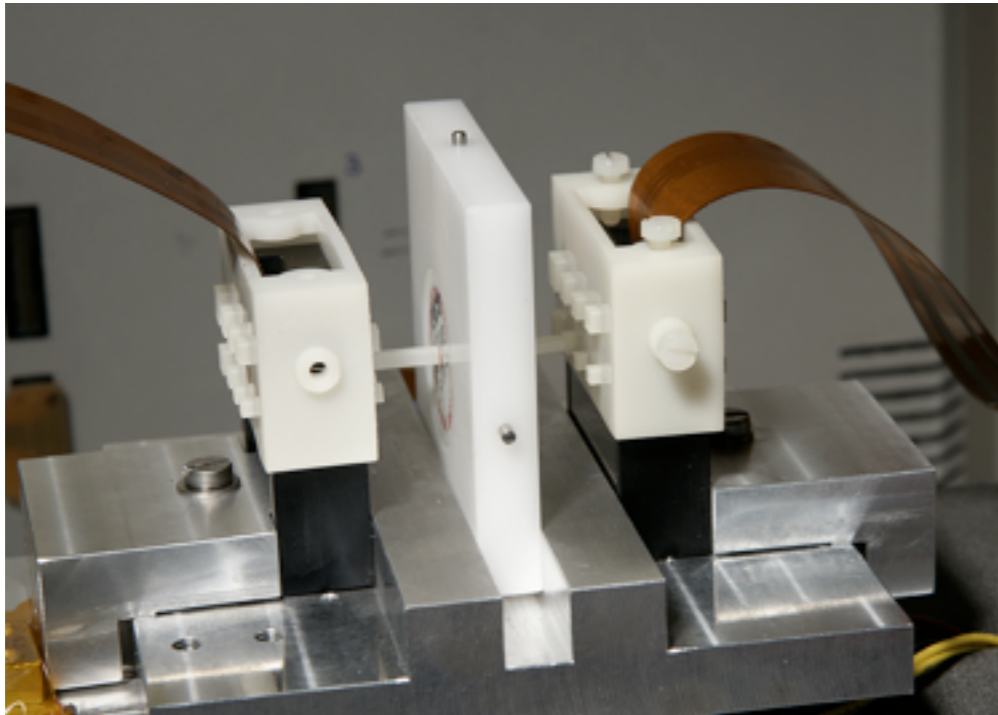
AGILE <b>LYSO</b>	~ 2000	~ 1700	~ 1400
SIPAT <b>LSO</b> [*]	~ 1600	~ 1400	~ 1000
SIPAT <b>LSO:Ca</b>	~ 1300	~ 1100	~ 900

[\*] = plots

~ 1000 - 1500 pe's @ 511 keV  
different saturation response depending on the adopted SiPM type

# Timing properties of different crystals

- different types of crystals
- pairs of crystals tested with **digital SiPM (Philips)**
- direct comparison of coincidence time resolution



## measured CRT

**[446 +/- 5.2] ps**

**[329.7 +/- 1.5] ps** **25% improvement wrt undoped**

**[228.1 +/- 1.5] ps** **30% improvement wrt bare**

LSO Ca-codoped

1.5 x 1.5 x 12 mm<sup>3</sup> - Sipat **LSO:Ce**

← 1.5 x 1.5 x 12 mm<sup>3</sup> - Sipat **LSO:Ce : Ca**

1.5 x 1.5 x 12 mm<sup>3</sup> - Sipat **LSO:Ce : Ca + wrapped** crystal (ESR) and optical coupling between crystals and photosensors (**grease**)

**LSO Ca-codoped are better in terms of timing BUT DIFFICULT TO PROCURE in large quantity**

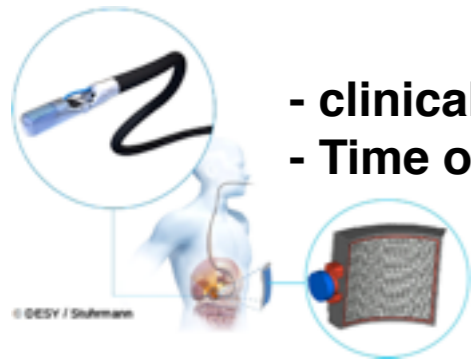
# Readout ASIC chip

measure time and energy  
on individual channels  
with very good timing perfs

Out of the many existing SiPM readout chips options :

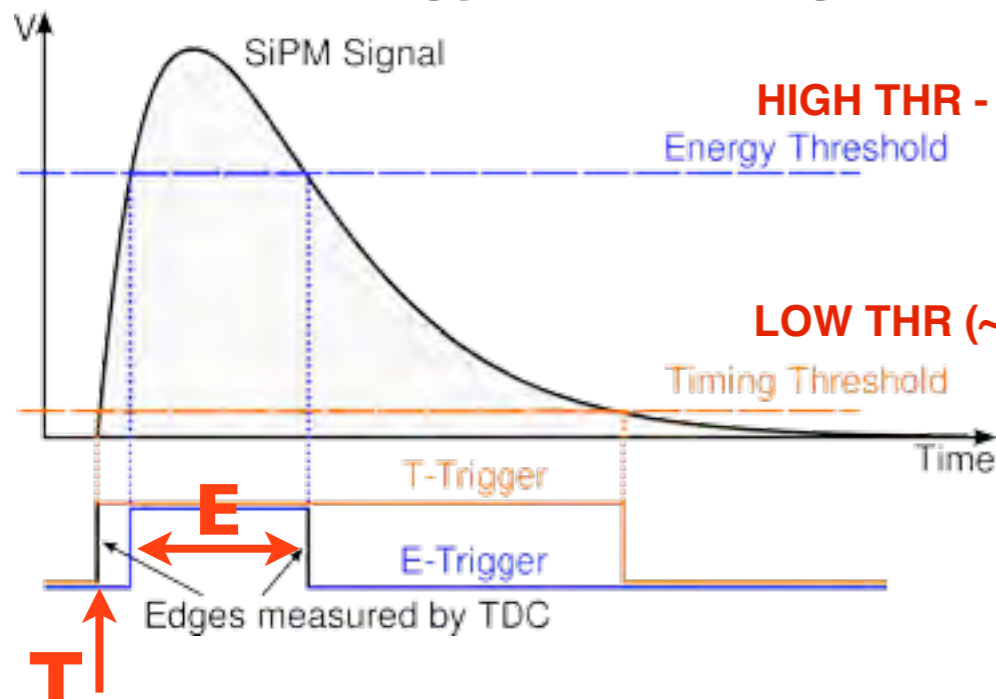
- **ToFPET(v1) ASIC** (developed at LIP - Lisbon) Rolo et al, JINST8 C02050
- **STiC v3.1 ASIC** (developed at KIP - Heidelberg) Harion et al, JINST9 C02003

Both developed within the Endo-TOFPET-US project



	EndoTOFPETUS	SAFIR
readout for SiPM and Xtals matrices	✓	✓
measure time and energy	✓	✓
timing resolution	✓ excellent (CRT ~ 200 ps FWHM)	✓ very good (CRT < 500 ps FWHM)
high channel density	✓	✓
low power consumption	✓	✓
high rate capabilities		✓

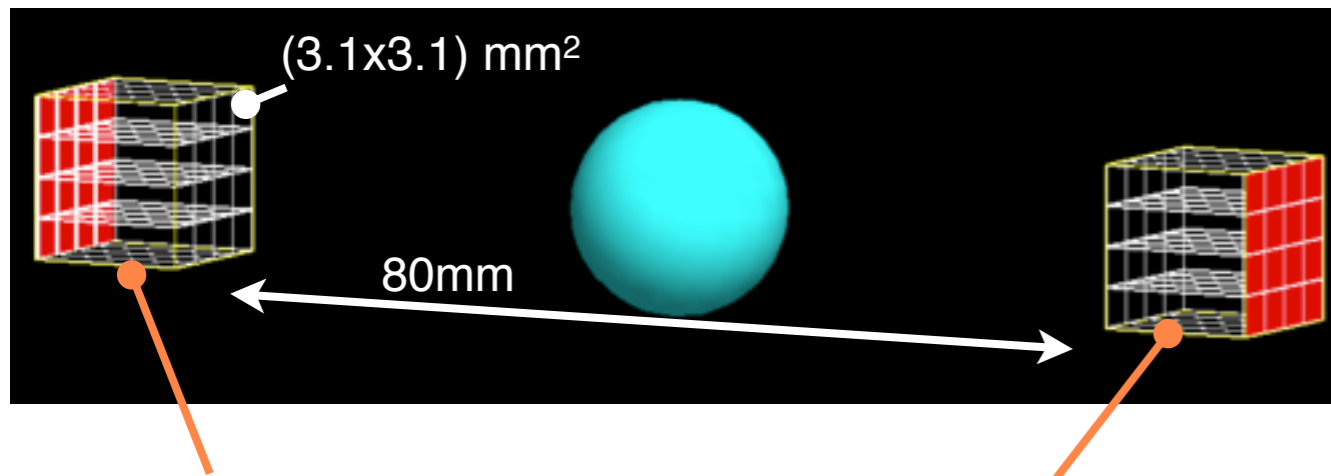
## Energy and Timing measurements through the Time Over Threshold logic



64 channels/ASIC

mixed mode : analogue FE (ampli, disci) + digitization / LVDS output  
same logic - different implementations

# High rate test with TOFPET and STiC ASICs



at University Zurich Hospital  
(daily 18-F production)

- Activity : ball phantom [ $\varnothing = 11\text{mm}$ ] filled with FDG [ $t_{1/2}$  18-F  $\sim 120$  mins]
- Activities up to 500 MBq

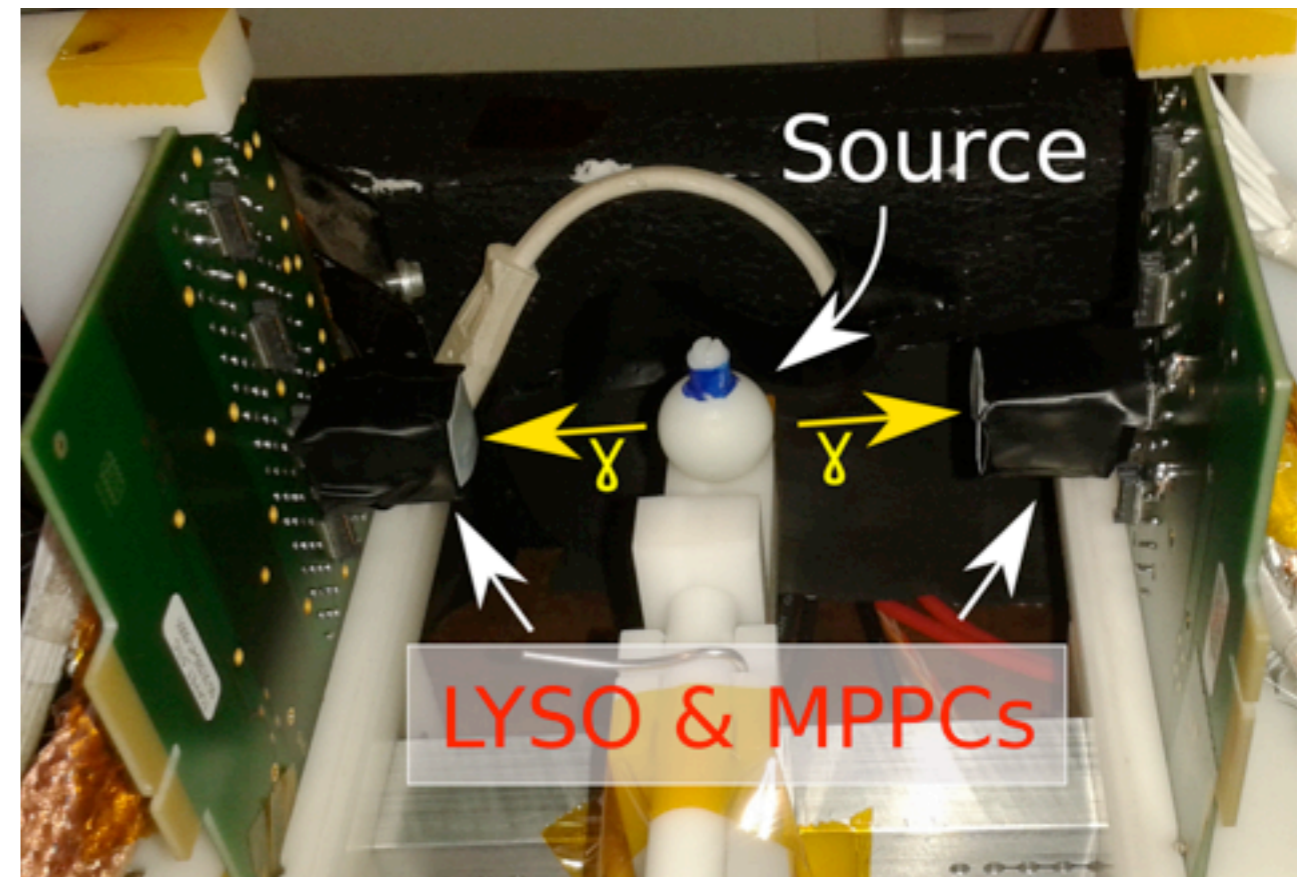
- **2 matrices [xtals + SiPM arrays] - 4x4 channels**

- Hamamatsu S12642-0404PB-50 : 4x4 ch, TSV, 3x3 mm<sup>2</sup> sensor size, 3.2 mm pitch
- LYSO crystals (Agile) : 4x4 xtals, (3.1 x 3.1 x 12) mm<sup>3</sup> each, ESR wrapping / separation (100  $\mu\text{m}$  thick)

**i.e. existing commercial components - different form factors and distances wrt SAFIR reference design**  
**- reduced nr of channels/chip**

- operated in coincidence
- same matrices used alternatively for the TOFPET and the STiC setup
- 2 identical parallel setups in a thermal box

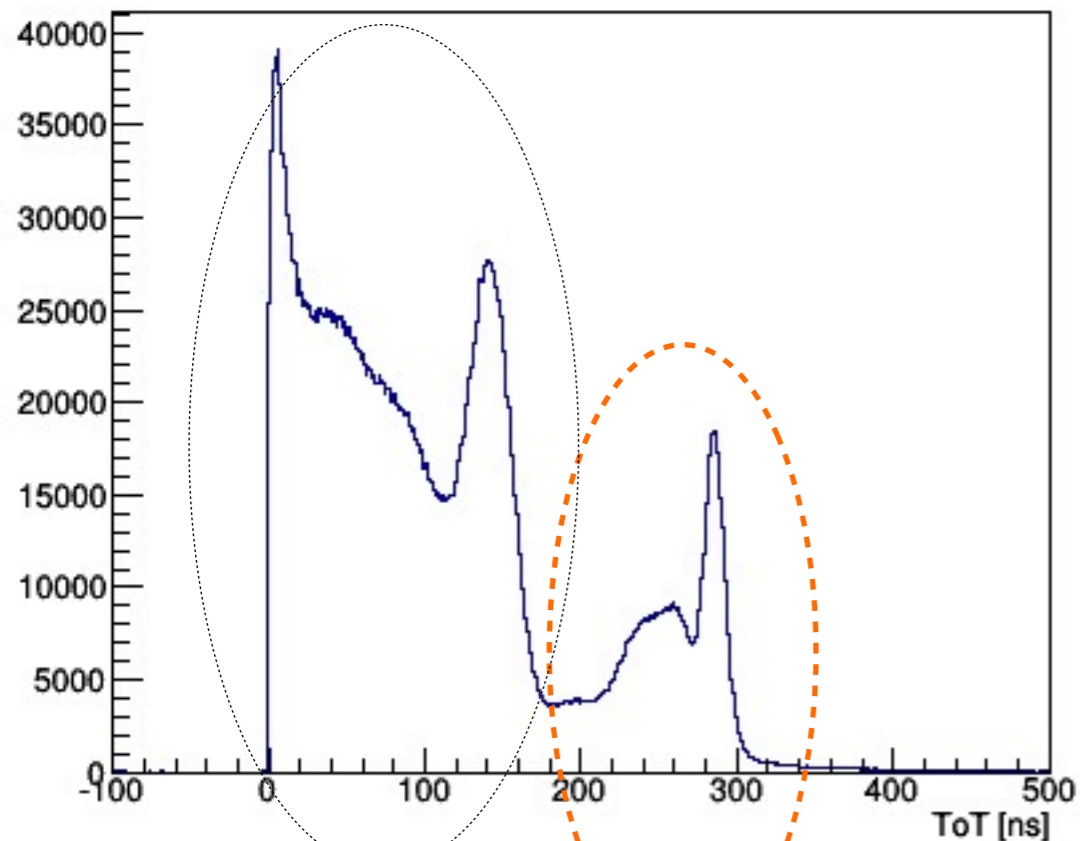
- ToT spectrum
- Rate capabilities
- CRT performance



# TOFPET performance : ToT and Rate

## Time Over Threshold

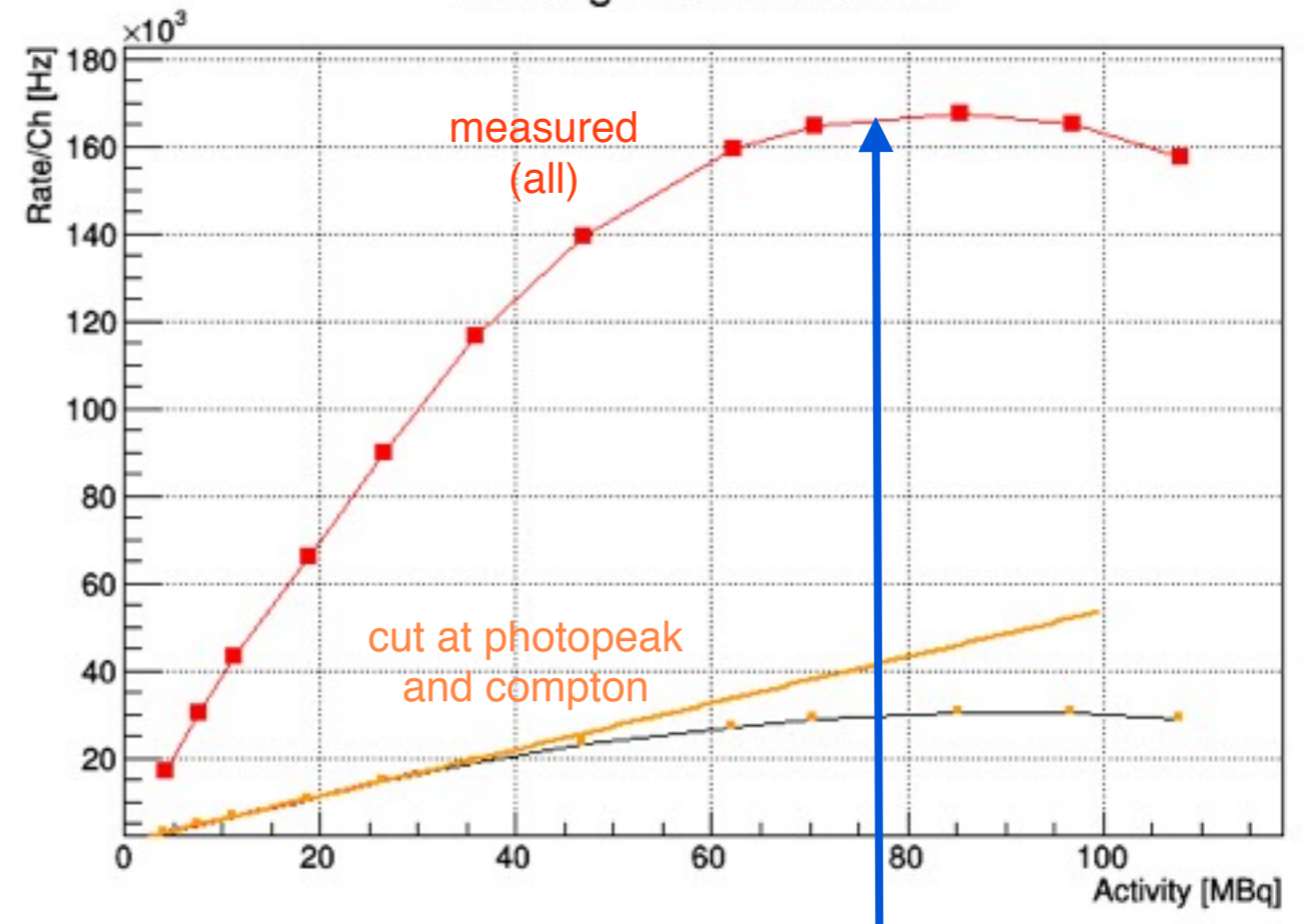
ToT - single channel



Low Energy contribution due to important cross talk effect in the crystal matrix

## Rate performance

Average Rate/Channel



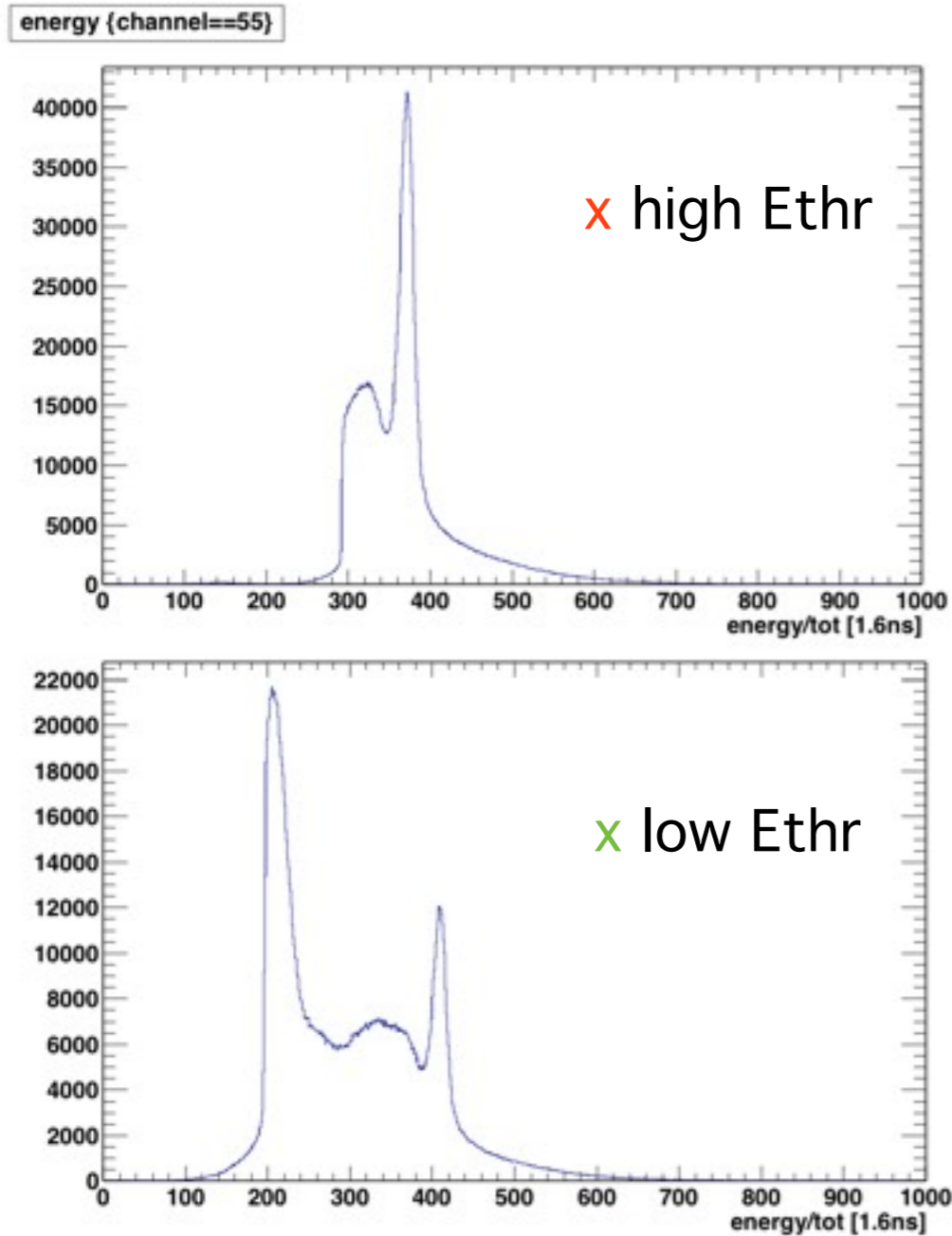
**500 MBq SAFIR-equivalent**  
(scaled by size of xtals and F2F distance)

- up to 160 kHz/channel
- then : saturation effect
- not linear anymore at SAFIR equivalent point
- low energy contribution significantly impacts the total rate/channel

# STiC performance : ToT and Rate

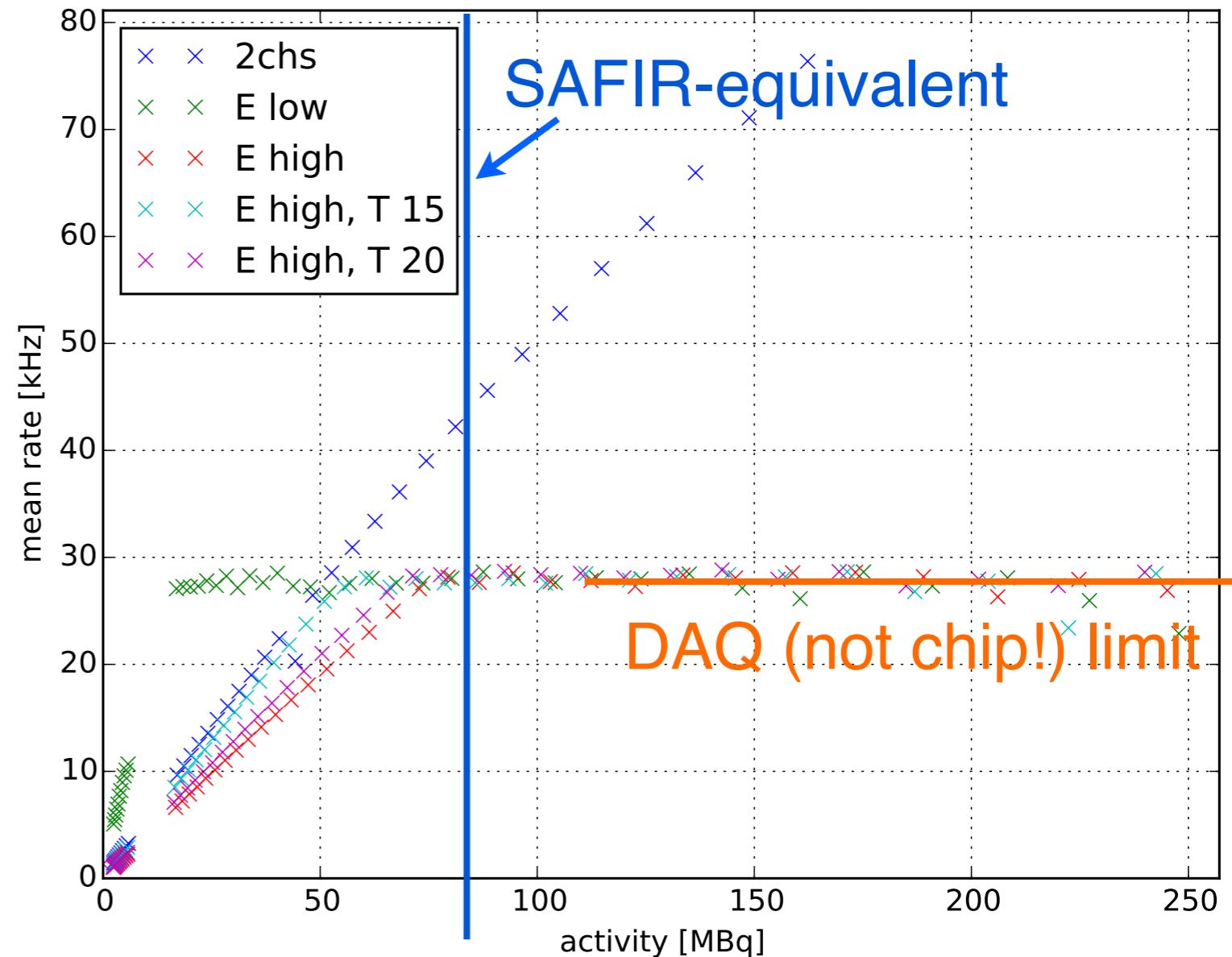
## Time Over Threshold

Flexibility in adjusting THRESHOLDS over a broad range!



+ **linearization** circuitry in the ToT

## Rate performance



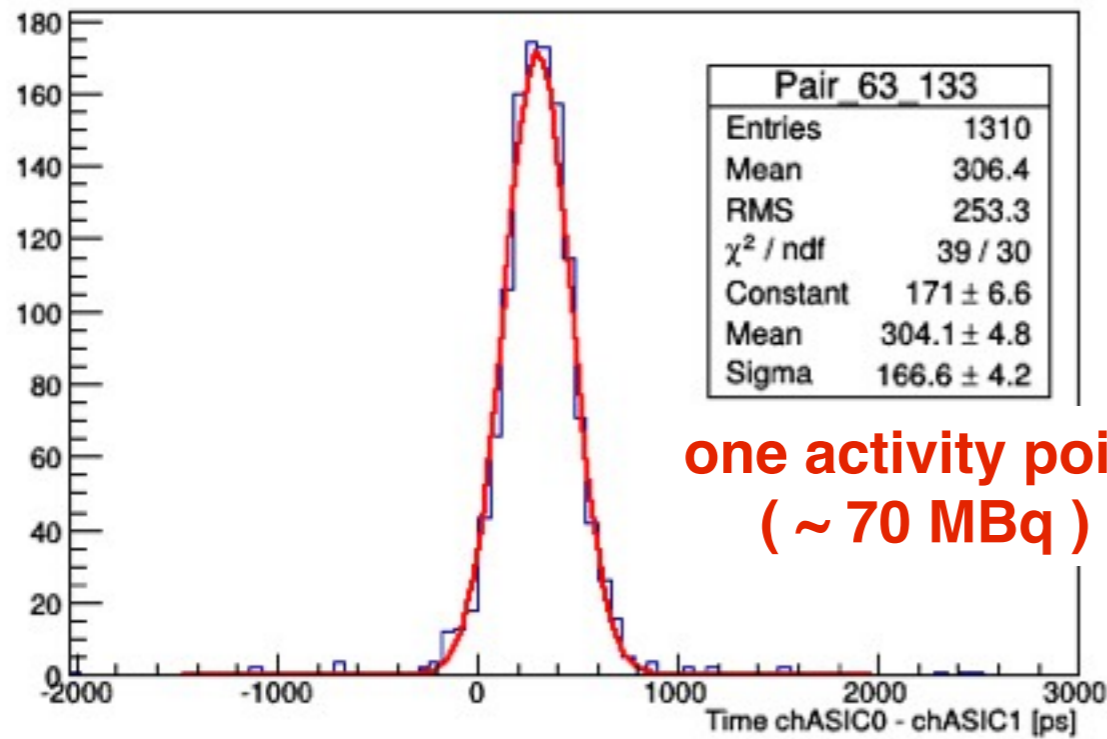
- DAQ (**USB link**) limit  $\sim 700$  kHz (total)
- different Ethr in ToT  $\Rightarrow$  different slopes in rate/ch vs activity
- 2 channels test :
  - demonstrates high rate chip capabilities ( $\gg$  SAFIR req)
  - $\sim 40$  kHz/channel at SAFIR-equivalent (as from MC)



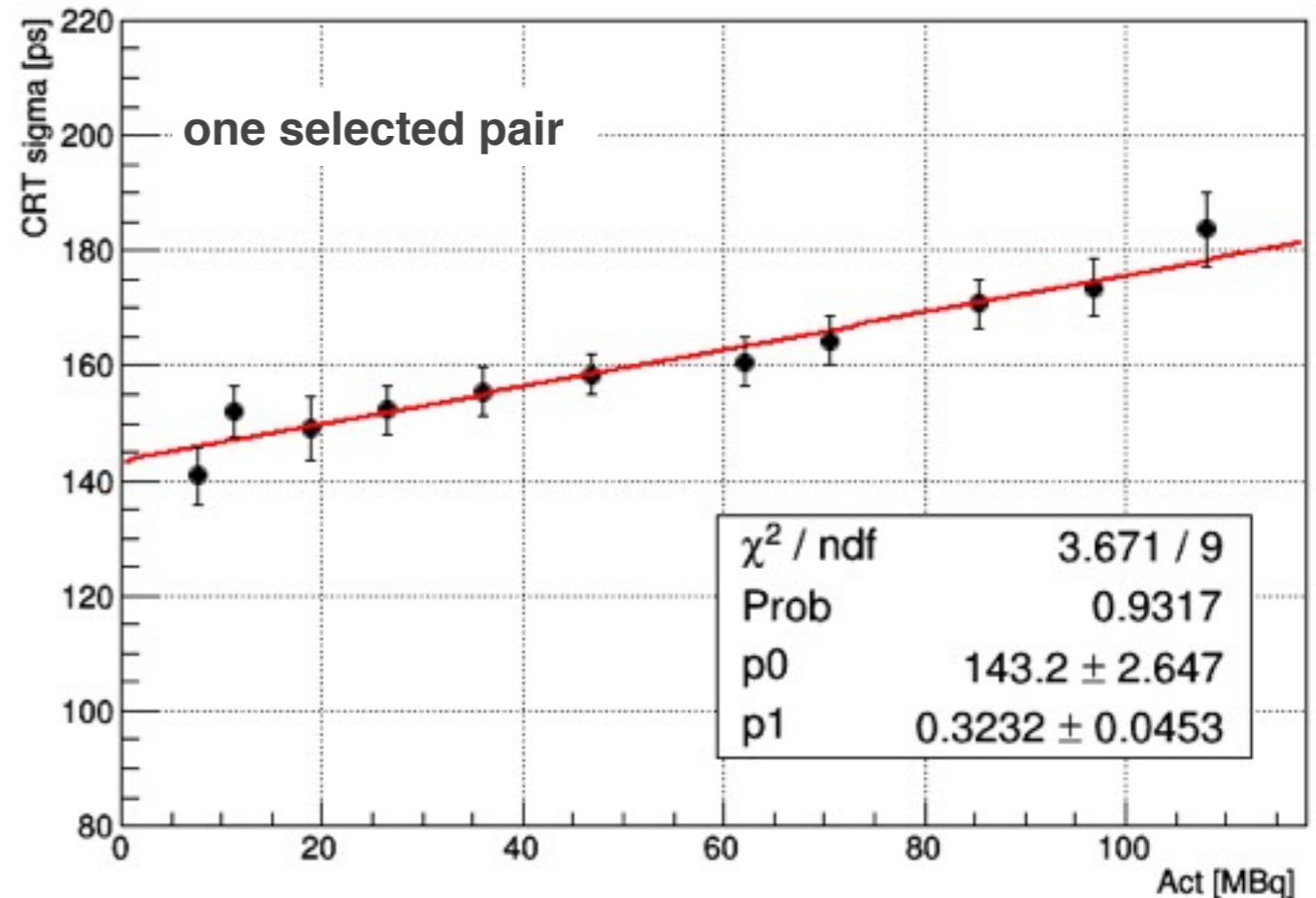
# TOFPET performance : CRT

## Coincidence Time Resolution (CRT) - one selected pair

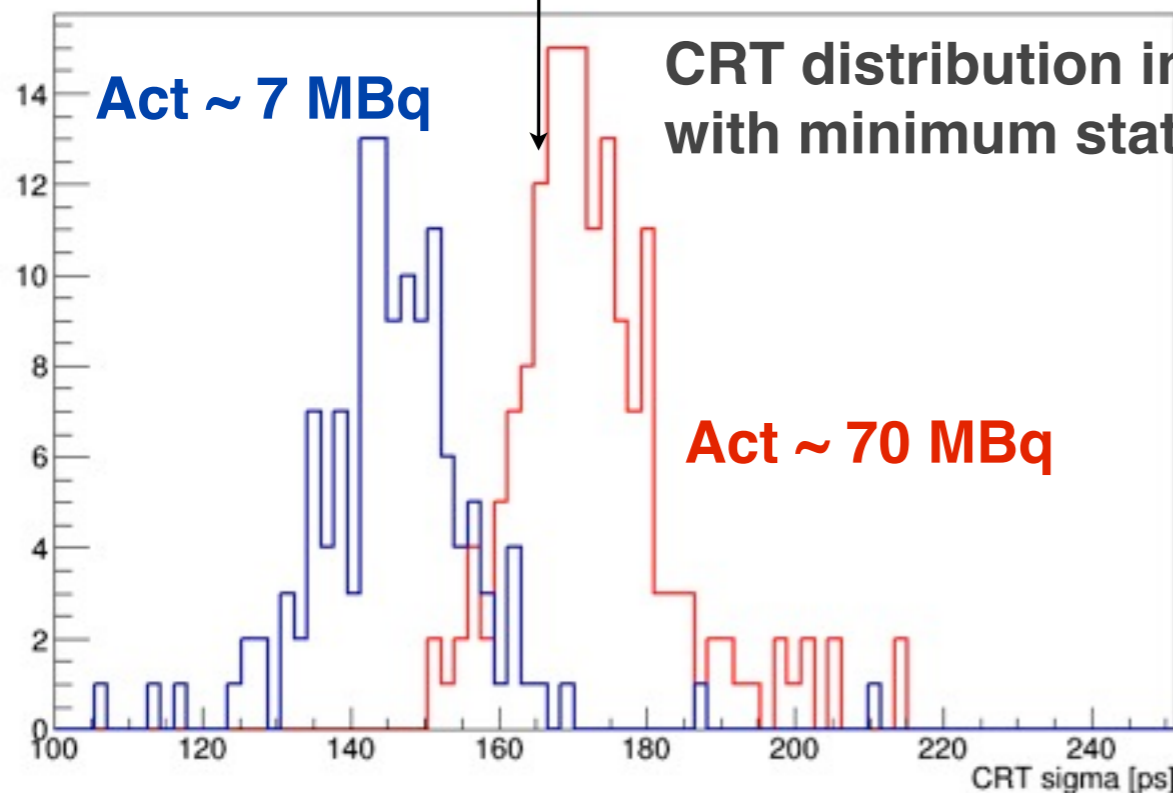
CRT Pair\_63\_133



one activity point  
( ~ 70 MBq )



CRT distribution (stat>100)



Act ~ 7 MBq

CRT distribution in all pairs  
with minimum statistics

Act ~ 70 MBq

## CRT performance

linear degradation of CRT with increasing activities

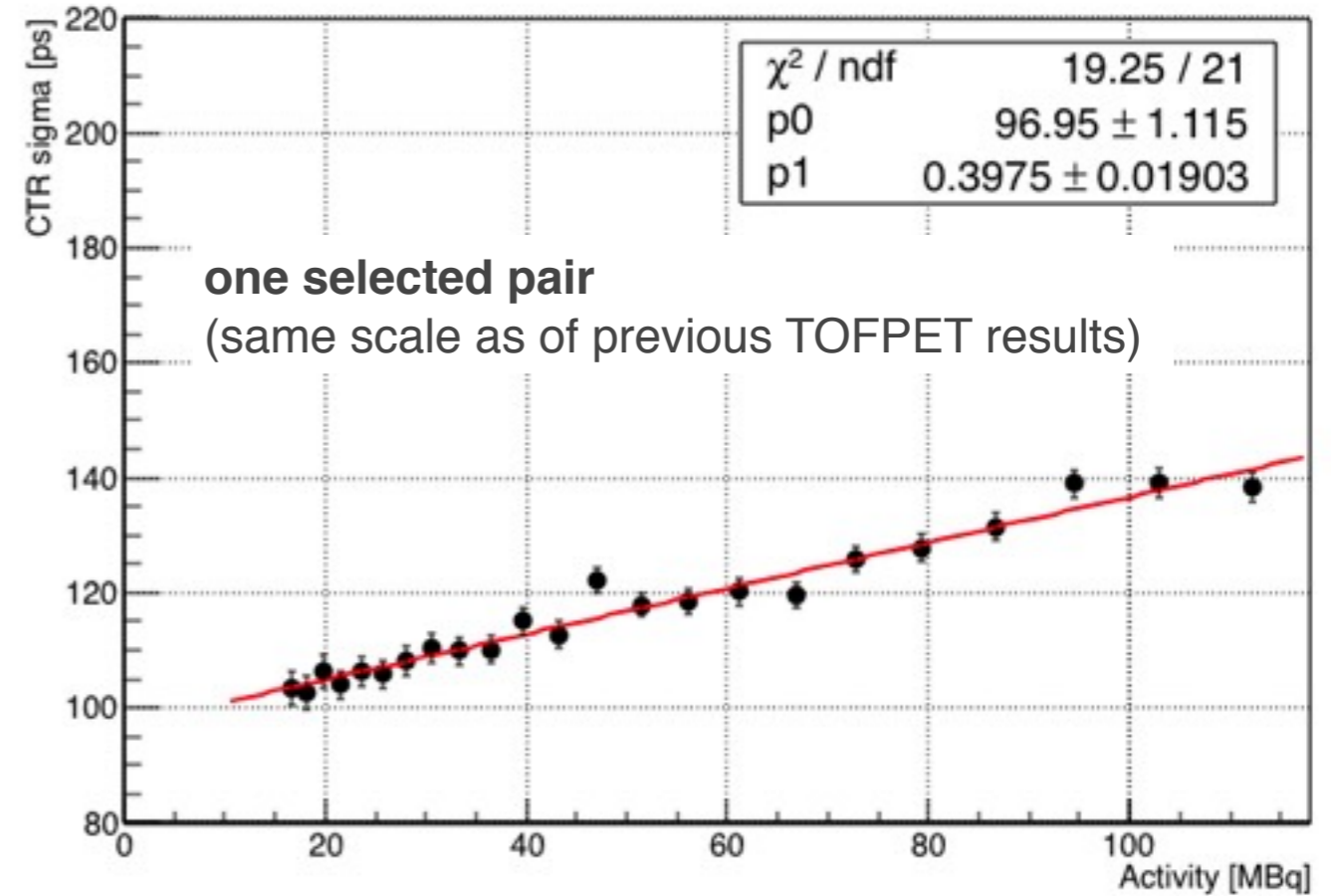
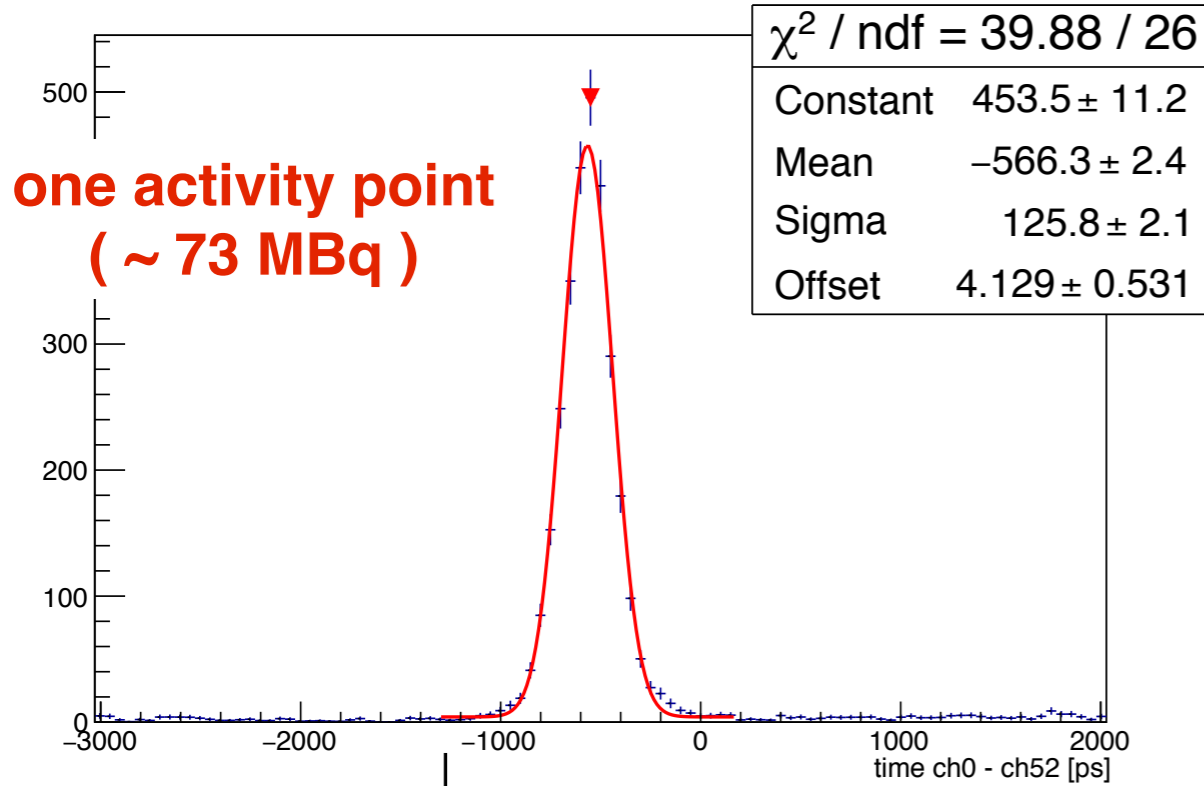
$\langle \text{CRT} \rangle @ \text{Act} \sim 7 \text{ MBq} \Rightarrow 330 \text{ ps FWHM}$

$\langle \text{CRT} \rangle @ \text{Act} \sim 70 \text{ MBq} \Rightarrow 400 \text{ ps FWHM}$   
[ ~ 500 MBq SAFIR-equivalent ]

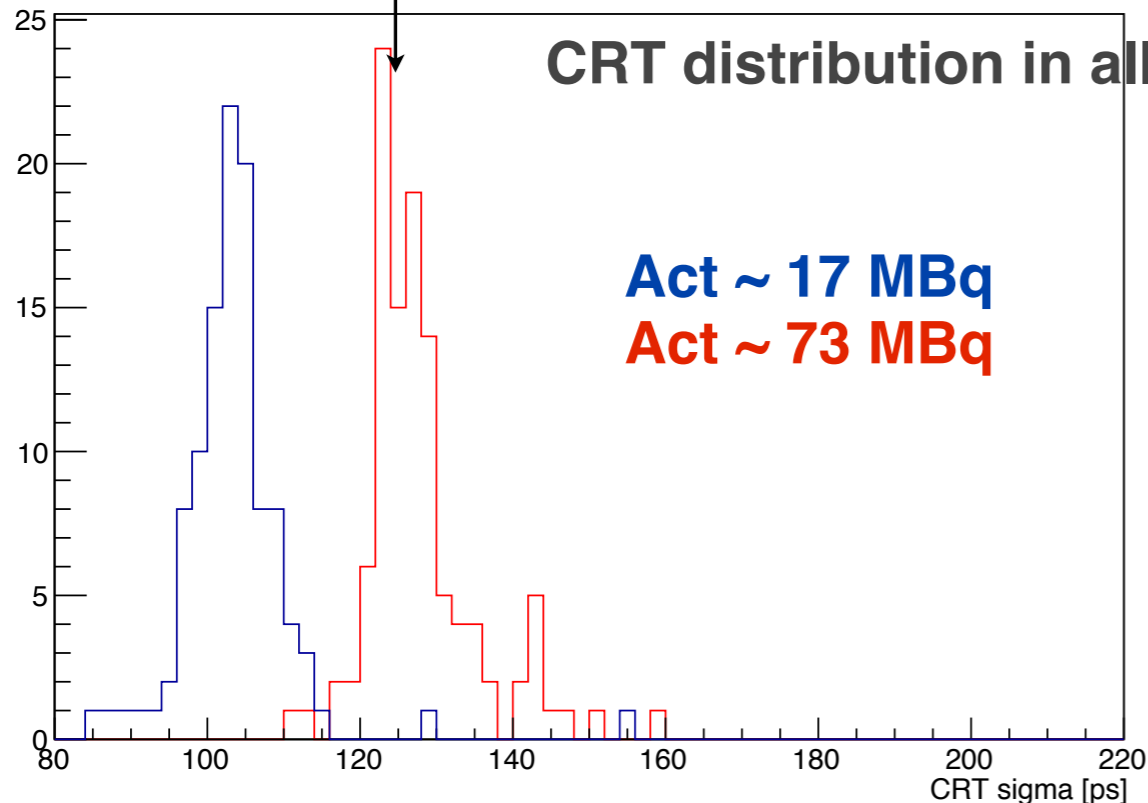
# STiC performance : CRT

## Coincidence Time Resolution (CRT) - one selected pair

CRT Pair 0-52 at 72.8 MBq



CRT distribution in all pairs



## CRT performance

linear degradation of CRT with increasing activities

$\langle \text{CRT} \rangle @ \text{Act} \sim 17 \text{ MBq} \Rightarrow 240 \text{ ps FWHM}$

$\langle \text{CRT} \rangle @ \text{Act} \sim 70 \text{ MBq} \Rightarrow 300 \text{ ps FWHM}$   
 [~ 500 MBq SAFIR-equivalent]

# TOFPET and STiC as possible readout for SAFIR

## Results from the High Rate Test :

- **Significant low energy contribution in the ToT distribution**  
in the tested setup [Agile matrices + Hamamatsu SiPM] (**cross-talk effect btw xtals**)
- Need to cut on those events  $\Leftrightarrow$  reduce bandwidth occupancy
- Need to have a **high validation threshold**:
  - **STiC(v3.1) : ok**
  - **TOFPET(v1) : no**
- **Rate capabilities :**
  - SAFIR requirement :  $\sim 40$  kHz/channel (with  $2 \times 2$  mm<sup>2</sup> detector size as in reference design)
  - **excellent rate performance ( $\gg$  SAFIR reqr.)** both for STiC(v3) and TOFPET(v1)
- **Coincidence Timing Resolution :**
  - SAFIR requirement : CRT  $\sim 300$ - $500$  ps FWHM
  - **very good CRT in the full range of explored activities**
    - **STiC(v3.1) CRT  $\sim 300$  ps FWHM** at 500 MBq SAFIR-equiv.
    - **TOFPET(v1) CRT  $\sim 400$  ps FWHM** at 500 MBq SAFIR-equiv.
  - Still under study : deterioration of the CRT with increasing activity
    - $\Delta\sigma/\Delta\text{Act} \sim 30$ - $40$  ps / 100 MBq (100 MBq in HighRateTest setup  $\sim 650$  MBq SAFIR)
    - but does not compromise the CRT perfs

**$\Rightarrow$  STiC is considered a valid candidate for SAFIR readout**

# PETA module

## alternative option for SAFIR

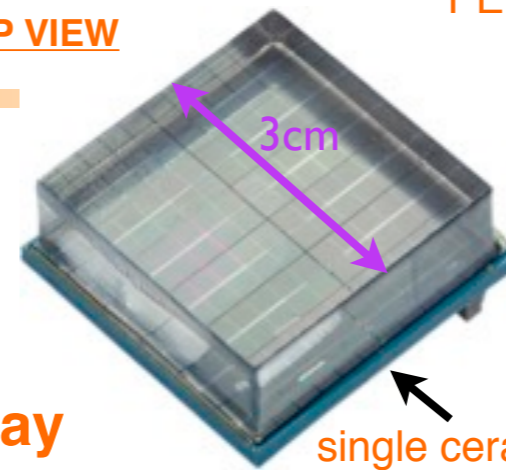
- compact module for TOF in PET [crystals, SiPM array, RO chip]

I. Sacco et al: 10.1016/j.nima.2015.11.004 [in press]

- developed within the Sublima project
- based on the PETA chip

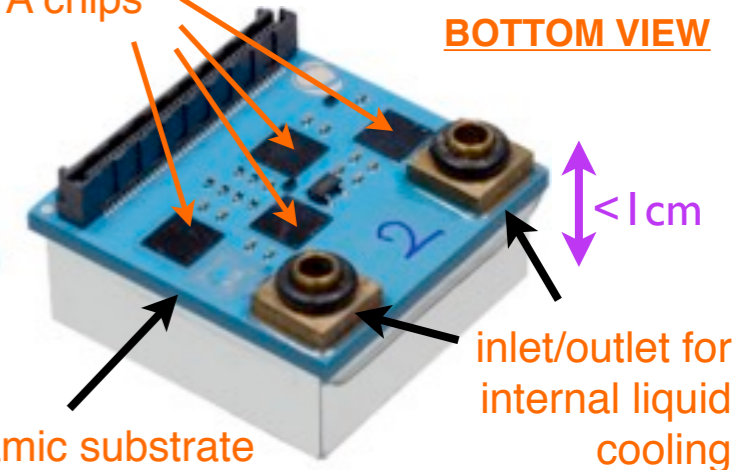
## Tests with high activity (one chip/module) 2 modules coincidences

TOP VIEW



PETA chips

BOTTOM VIEW



### SiPM array

- FBK (RGB-HD technology)
- 12x12 channels
- (2.25 x 2.25 x 10) mm<sup>3</sup>
- 2.5 mm pitch
- wire-bonded SiPM dies

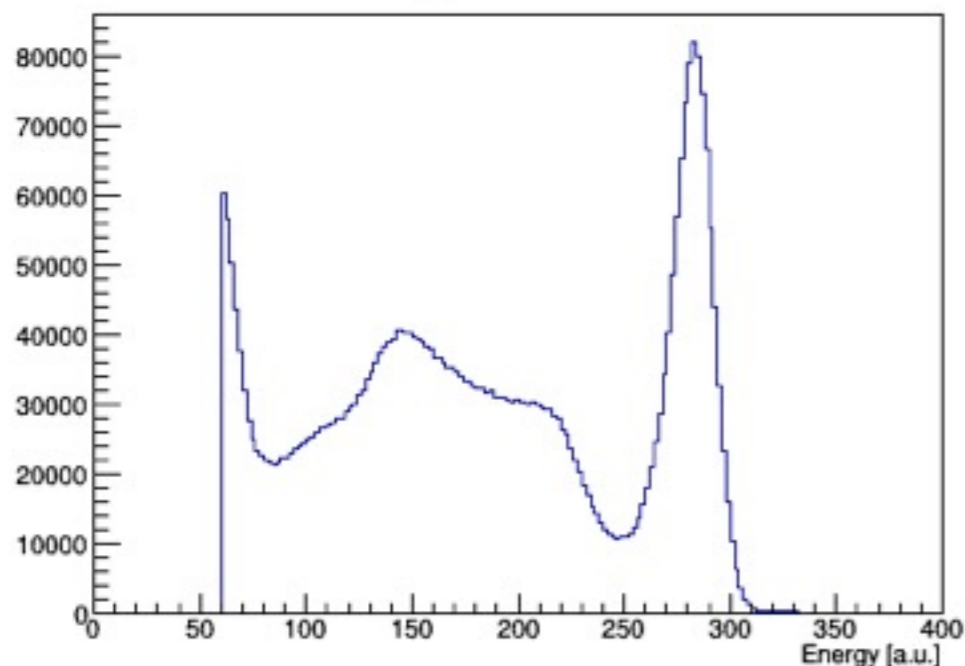
### Crystals

- LYSO + ESR/Alu/ESR

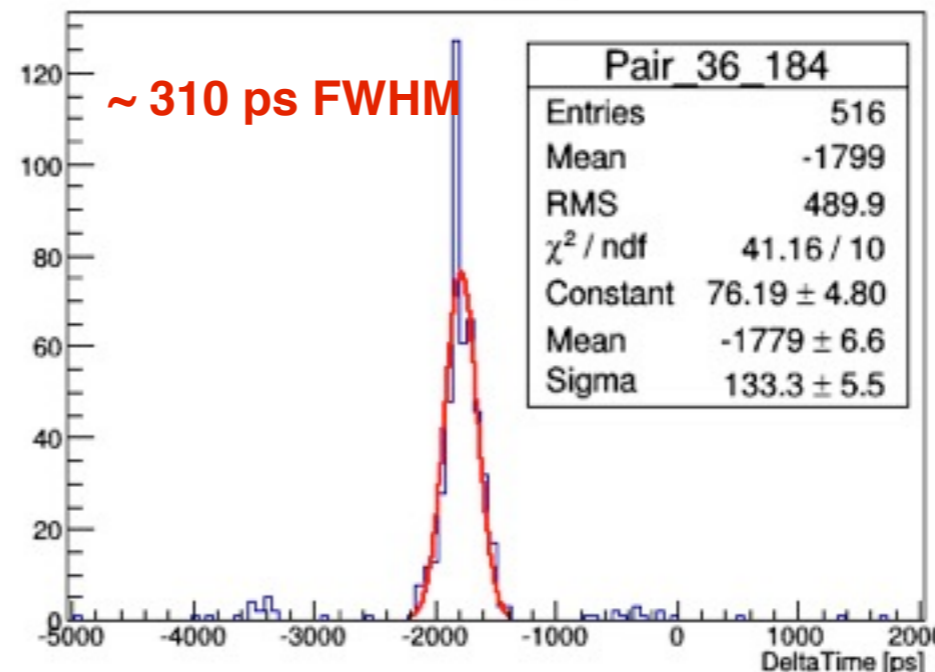
### Readout chip

- PETA5 chip (x4/module)
- Position Energy Time ASIC
- 32 channels / chip
- bump-bonded ASIC
- Time (discr + TDC)
- Amplitude (charge input integr.)

single channel



CRT single pair



although only by preliminary tests

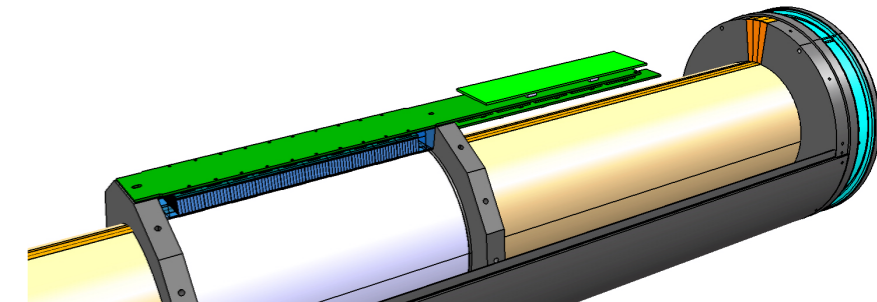
**PETA is considered a valid candidate for SAFIR readout**

# SAFIR future steps

Bruker BioSpin 70/30 MRI-scanner  
already commissioned and in use at ETH Zurich

## 1. Two small scale prototypes

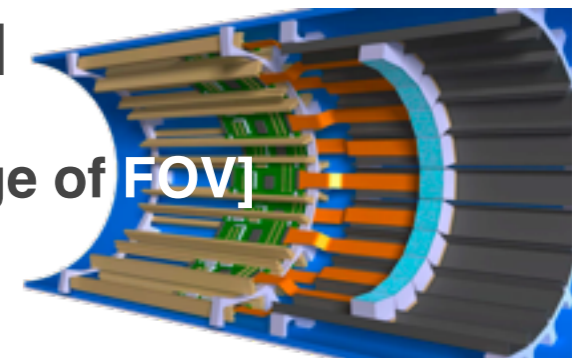
- two modules coincidence setups
  - in the final mechanical arrangement
  - inside the MR-bore
    - \* **PETA modules**
    - \* 2 modules (12x12)
    - \* xtal size : (2.25x2.25x12) mm<sup>3</sup>
    - \* **STIC chip RO**
    - \* 2 matrices (8x8)
    - \* xtals size : (2.1x2.1x12)mm<sup>3</sup>
    - \* “reference design”
- test high rate performance
- test full MR-compatibility
- now : building / commissioning the needed readout electronics
- expected - prototypes ready: May 2016 - tests : 2nd half 2016



The same support foreseen for the full system will be used in the two small scale prototypes

## 2. First full ring

- choice of the readout solution
- extension to one full ring [same geometry of xtals and SiPM as in prototype]
- development and tests of 4D reconstruction algorithms
- **full tomographic acquisitions for dynamic studies [but limited coverage of FOV]**
- expected : 2017



## 3. Final SAFIR detector

- design to be confirmed / tuned also on first full ring experience (e.g. maybe improve the spatial resolution with new developed detector heads)
- full commissioning ... towards ~ secs acquisitions!!!

# conclusions



# Conclusions

---

I have described the **SAFIR detector concept** and **its progress status**  
(software and hardware activities)

**SAFIR: unconventional detector for hybrid PET/MRI acquisition with the dedicated goal of dynamic and simultaneous imaging at unprecedented temporal resolutions**  
(target user: ETHZ/UniZh Institute of Biomedical Engineering)

Peculiarities of the detector :

**500 MBq activity** (wrt standard  $\sim 50$  MBq)

**excellent time resolutions : CRT  $\sim 300 - 500$  ps FWHM** (w/o being a TOF-PET)

**heavy usage of SiPM sensors**

(not peculiar to SAFIR, but standard nowadays in PET developments)

# Conclusions

I have described the **SAFIR detector concept** and its **progress status**  
(software and hardware activities)

**SAFIR: unconventional detector for hybrid PET/MRI acquisition with the dedicated goal of dynamic and simultaneous imaging at unprecedented temporal resolutions**  
(target user: ETHZ/UniZh Institute of Biomedical Engineering)

Peculiarities of the detector :

**500 MBq activity** (wrt standard  $\sim 50$  MBq)

**excellent time resolutions : CRT  $\sim 300 - 500$  ps FWHM** (w/o being a TOF-PET)

**heavy usage of SiPM sensors**

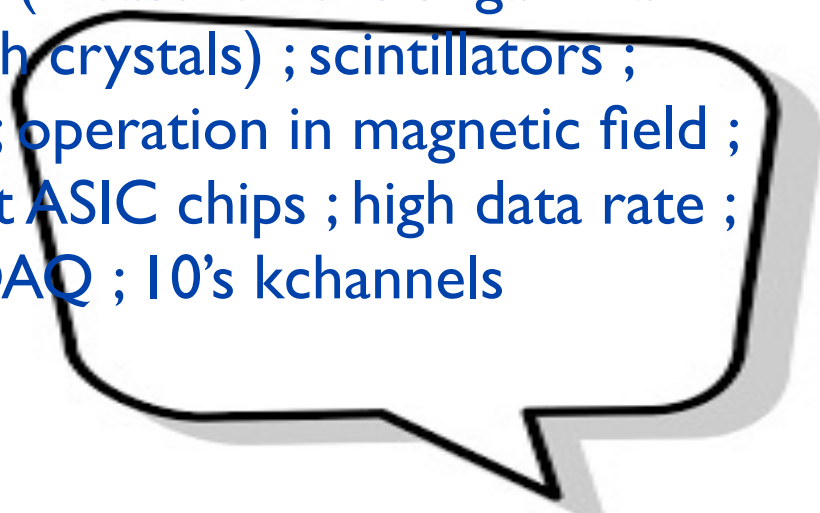
(not peculiar to SAFIR, but standard nowadays in PET developments)

What you were probably wondering at  
the beginning of this talk:



“ Small Animals??? PET???  
Magnetic resonance???  
What all this has to do with a  
HEP Department seminar ???”

Keywords of these slides :



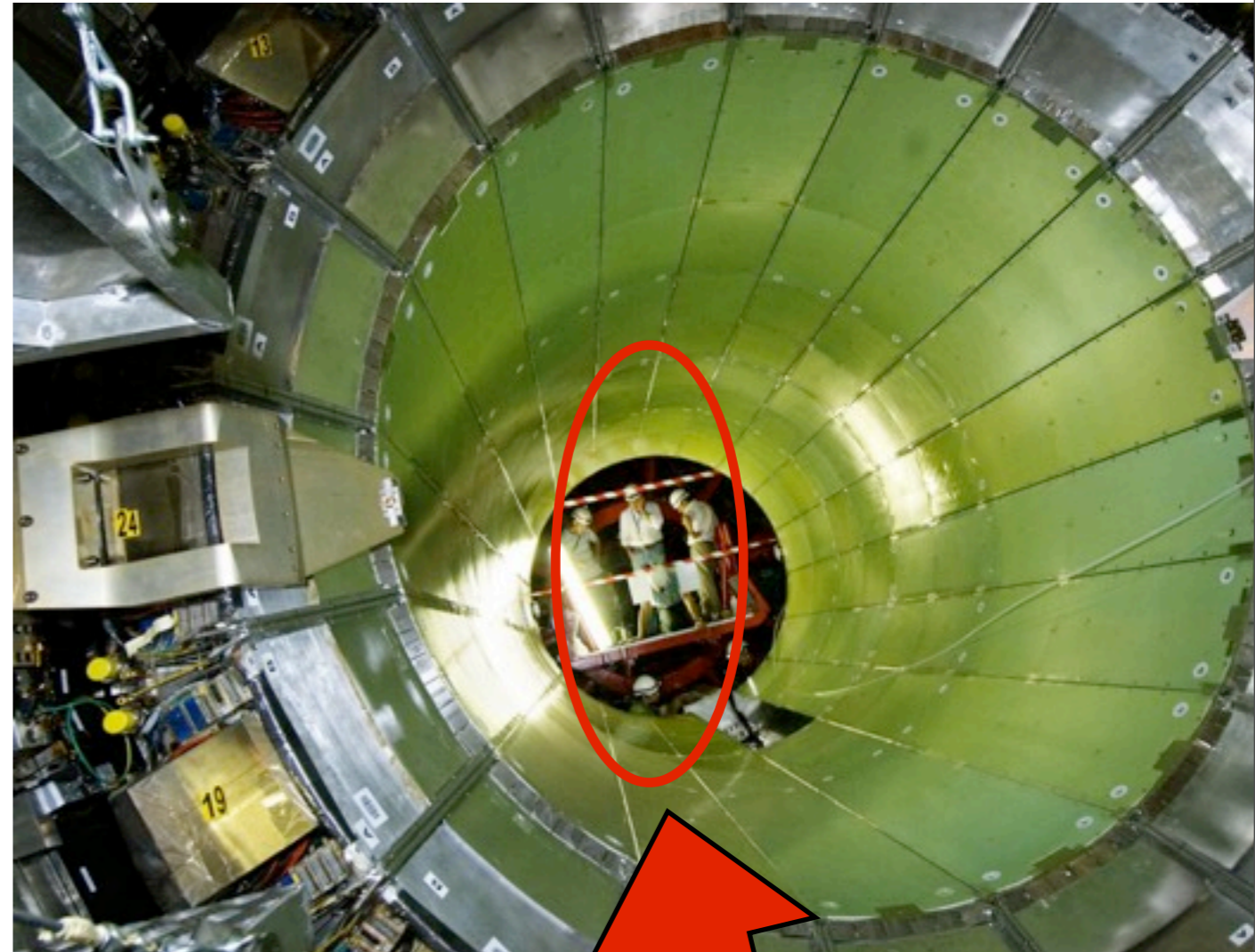
calorimetry (measurement of gamma  
energy with crystals) ; scintillators ;  
photosensors ; operation in magnetic field ;  
SiPM ; readout ASIC chips ; high data rate ;  
fast DAQ ; 10's kchannels



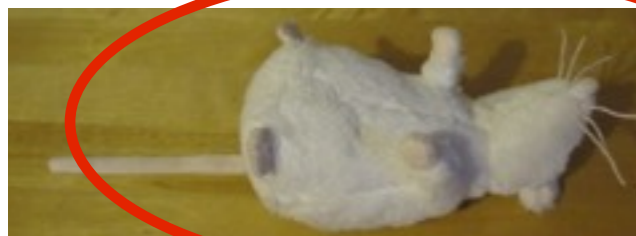
Inveon preclinical PET scanner



CMS ECAL barrel



many more similarities than  
it might look at first glance !



but not in the size!

# SAFIR collaboration

## **Institute for Particle Physics - ETH :**

R. Becker, C. Casella, D. Di Calafiori, G. Dissertori, L. Djambazov, M. Droge, C. Haller, A. Howard, M.Ito, P. Katheri, J. Fischer, W. Lustermann, U. Roeser

## **Institute for Biomedical Engineering - ETH:**

M. Rudin

## **Institute for Pharmacology and toxicology - University Zurich :**

A. Buch, G. Warnock, B. Weber

## **University of Valencia, IFIC :**

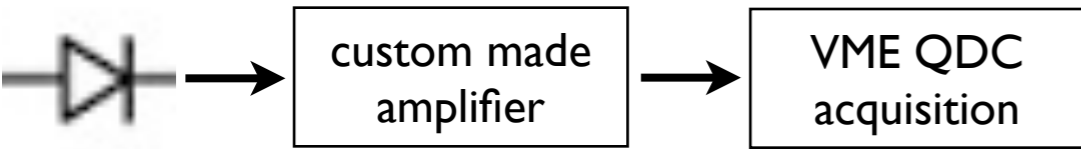
J. Oliver





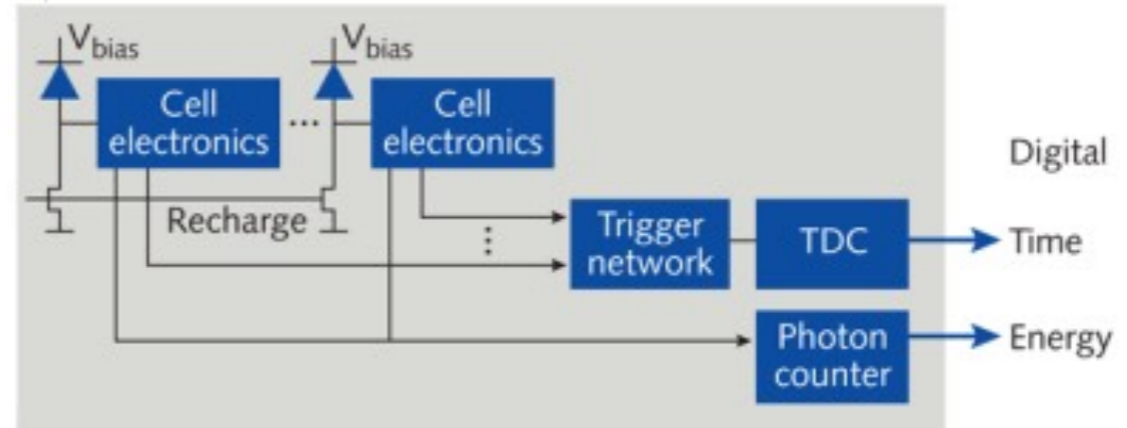
# Lab tools

- analogue readout chain



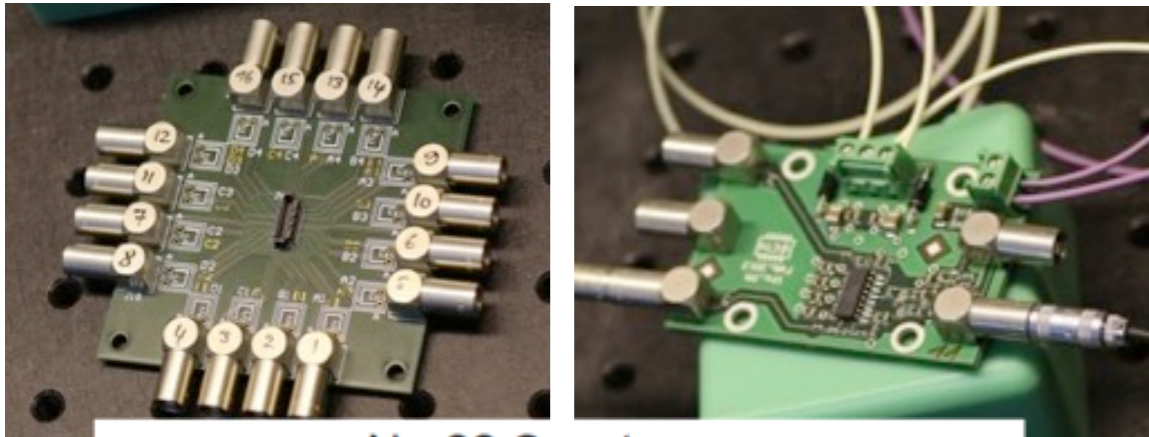
- Digital SiPM (Philips)

- fully digital implementation of SiPM
- the electronics for each cell implemented on the same Si substrate of the sensor
- high resolution TDC (19.5 ps resolution)

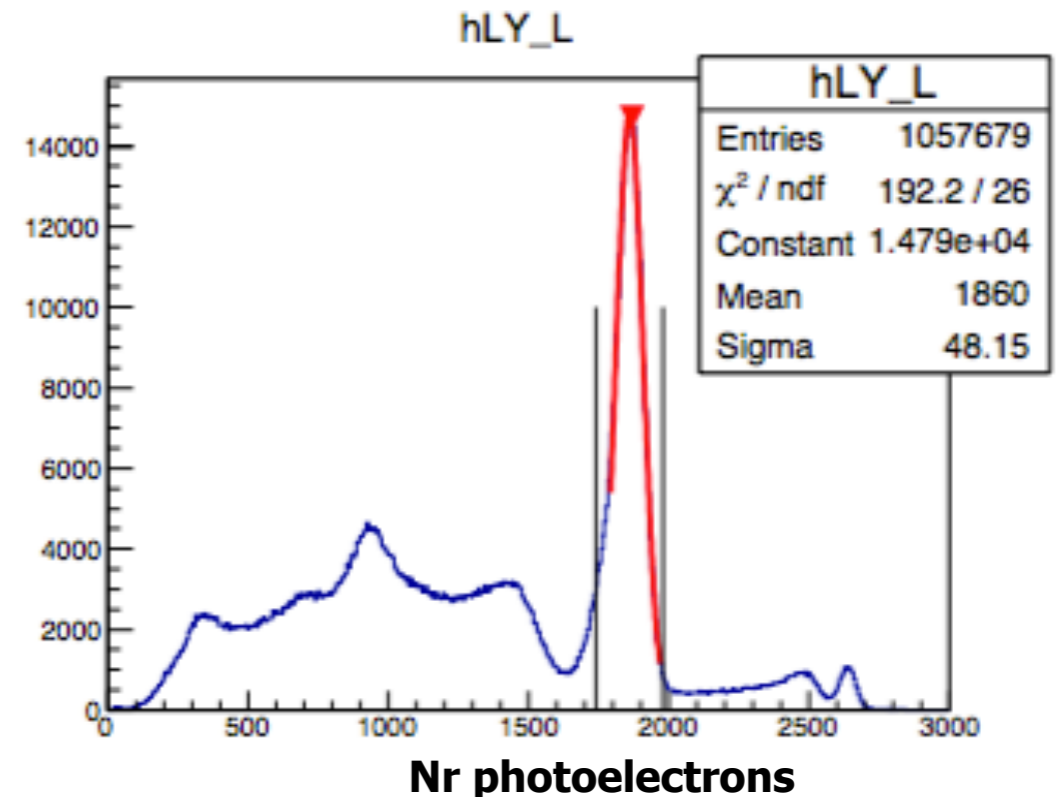
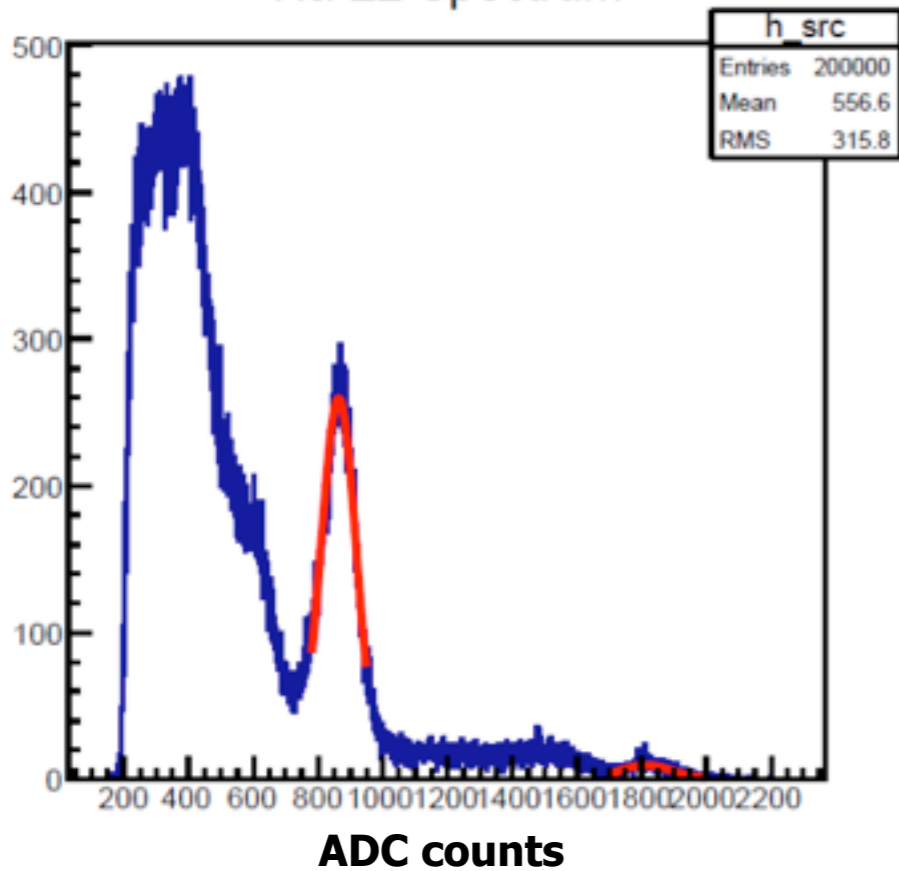


Very good tool for :

- photon counters
- coincidence timing measurements

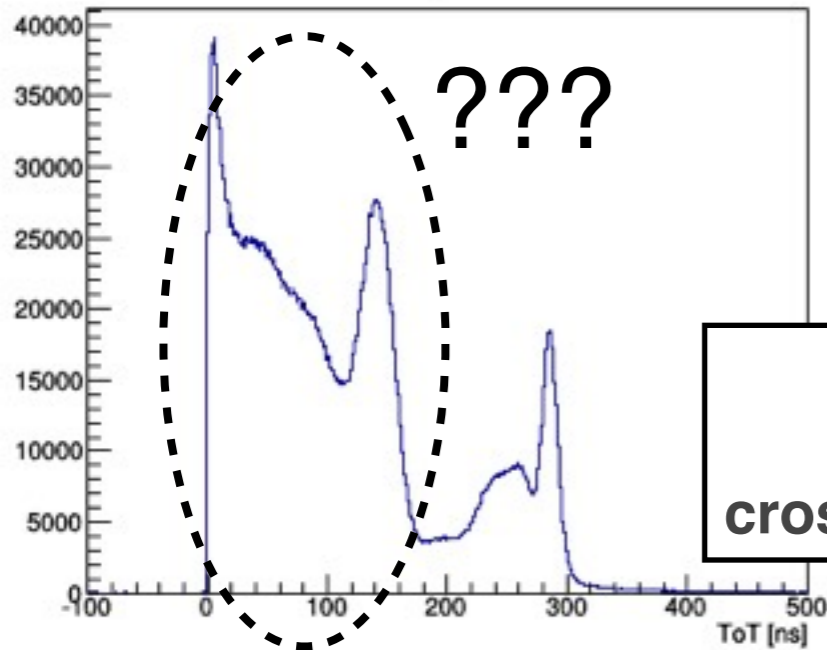


Na-22 Spectrum



# TOFPET performance : low energy contribution

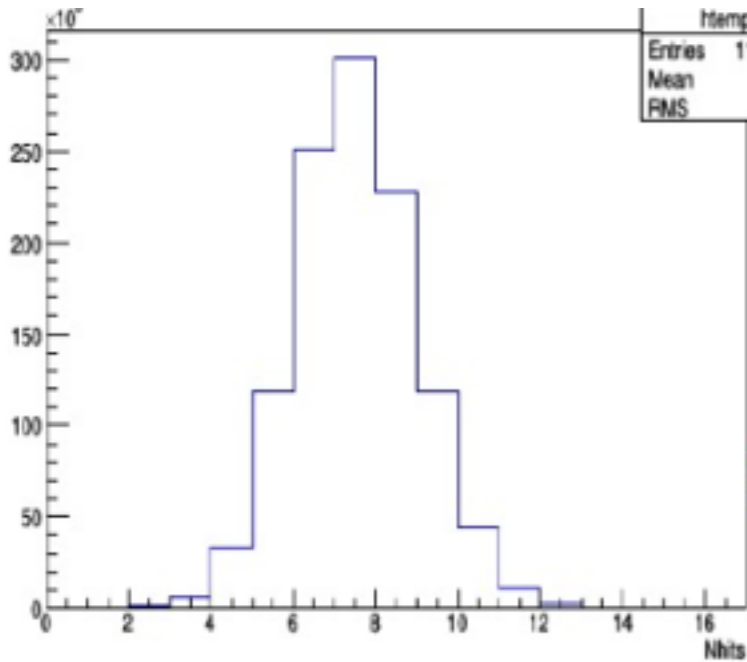
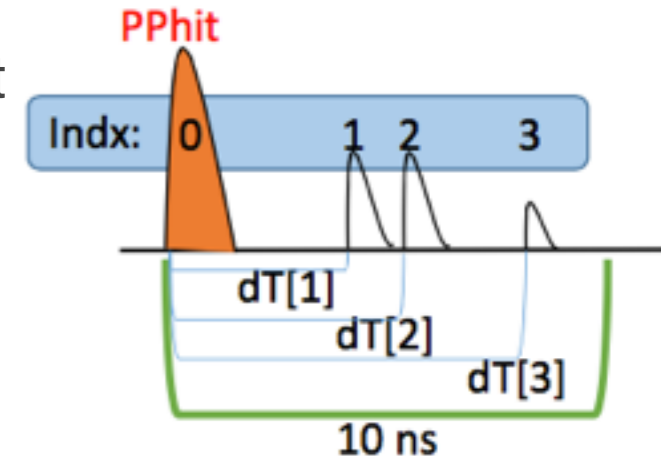
ToT - single channel



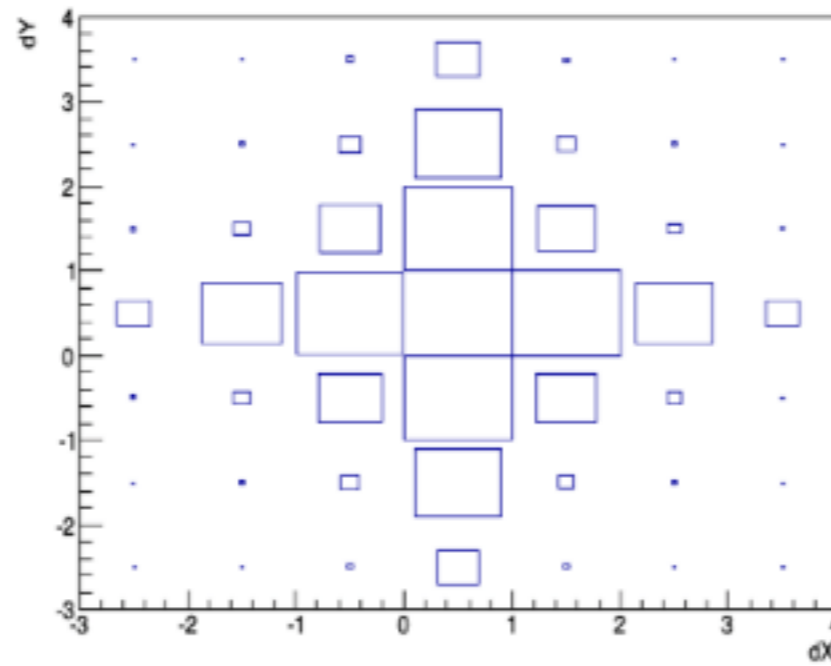
Low Energy contribution :  
due to a  
**cross talk effect in the crystal matrix**

Dedicated analysis on “coincidence events” :

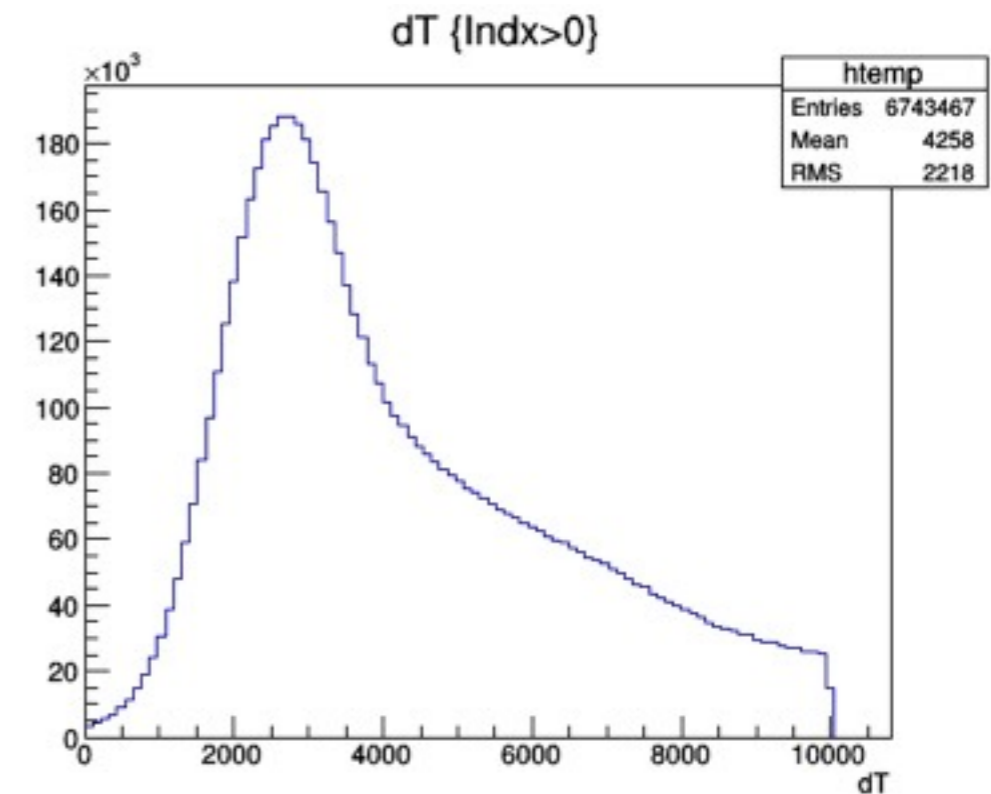
- 10 ns duration coincidence window
- within the same matrix
- started by a photopeak event



Average nr of hits  $\langle N \rangle \sim 7$

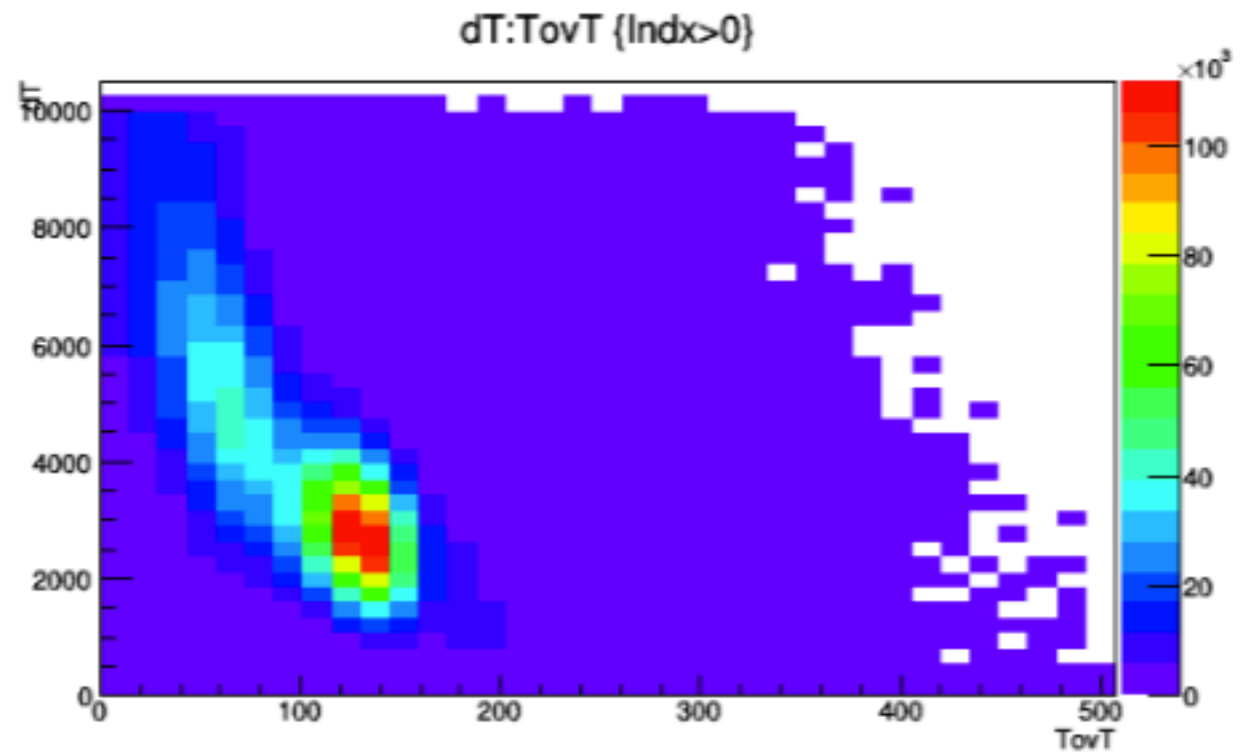
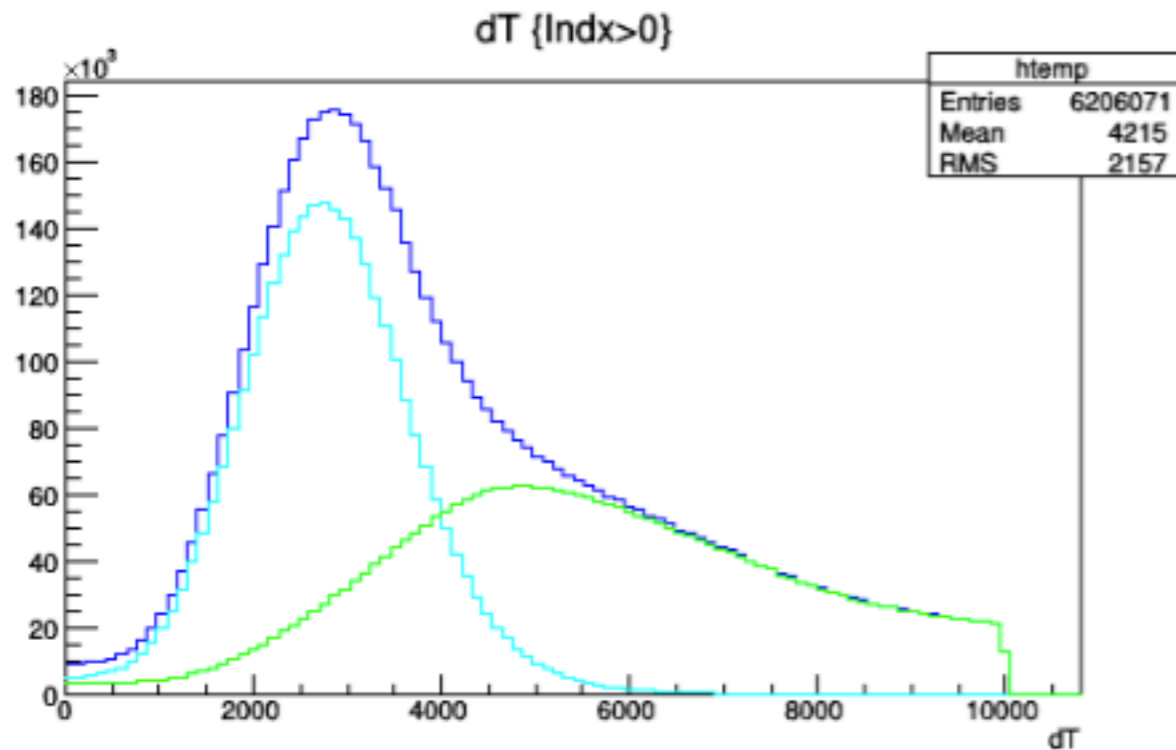
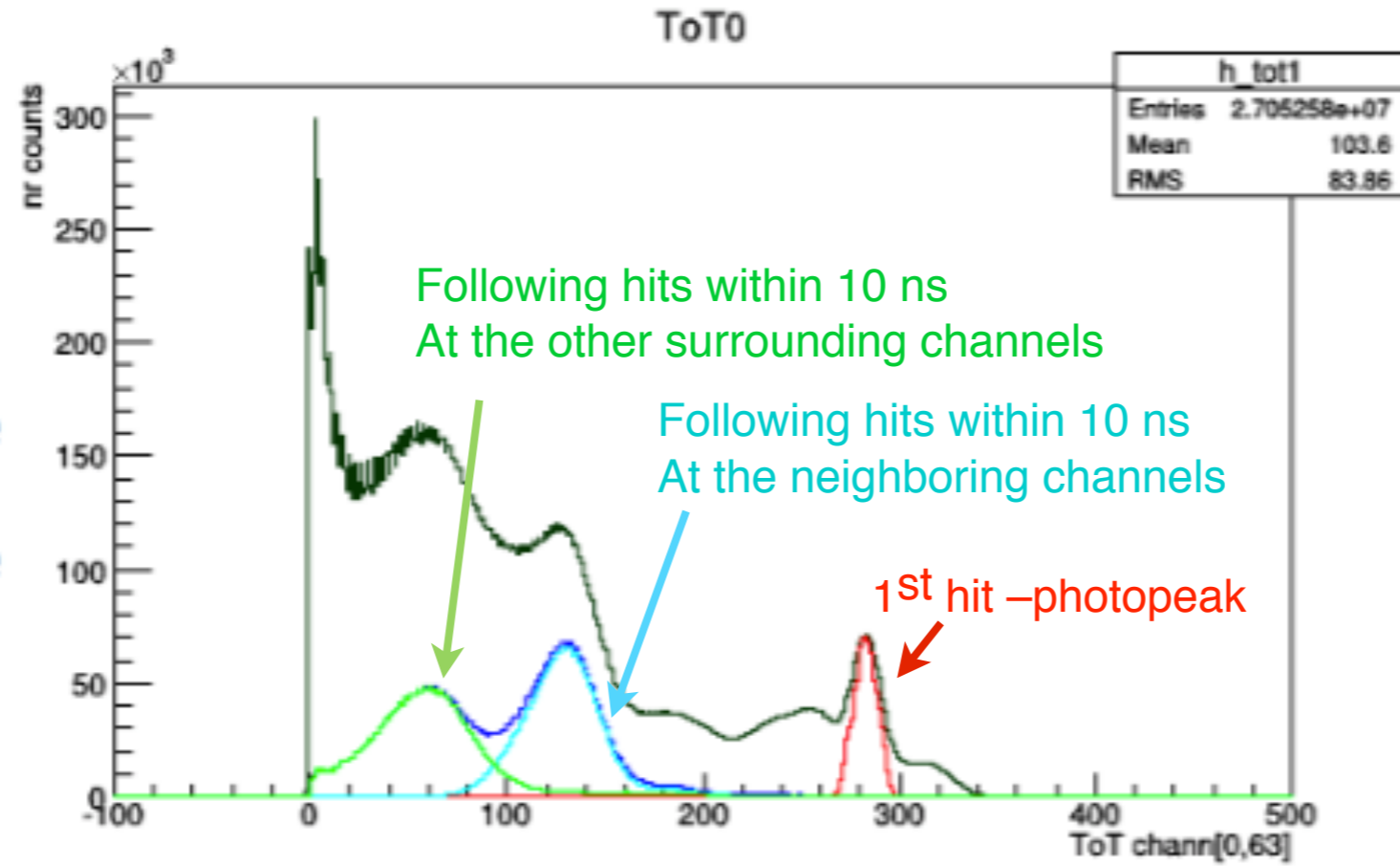


Geometrical correlation  
**direct neighbors**  
**neighbors to neighbors**



Time difference wrt photopeak hit

# TOFPET performance : low energy contribution

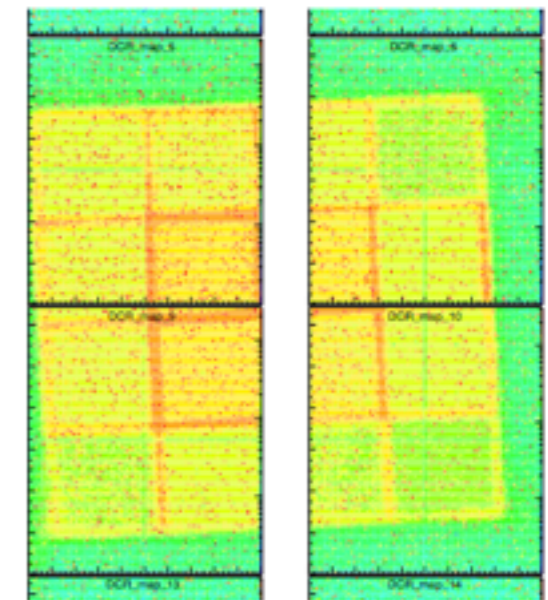
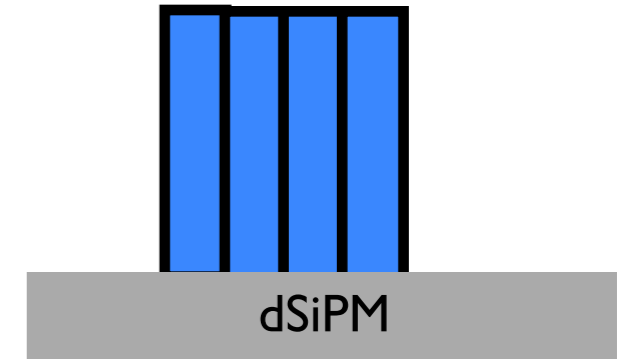
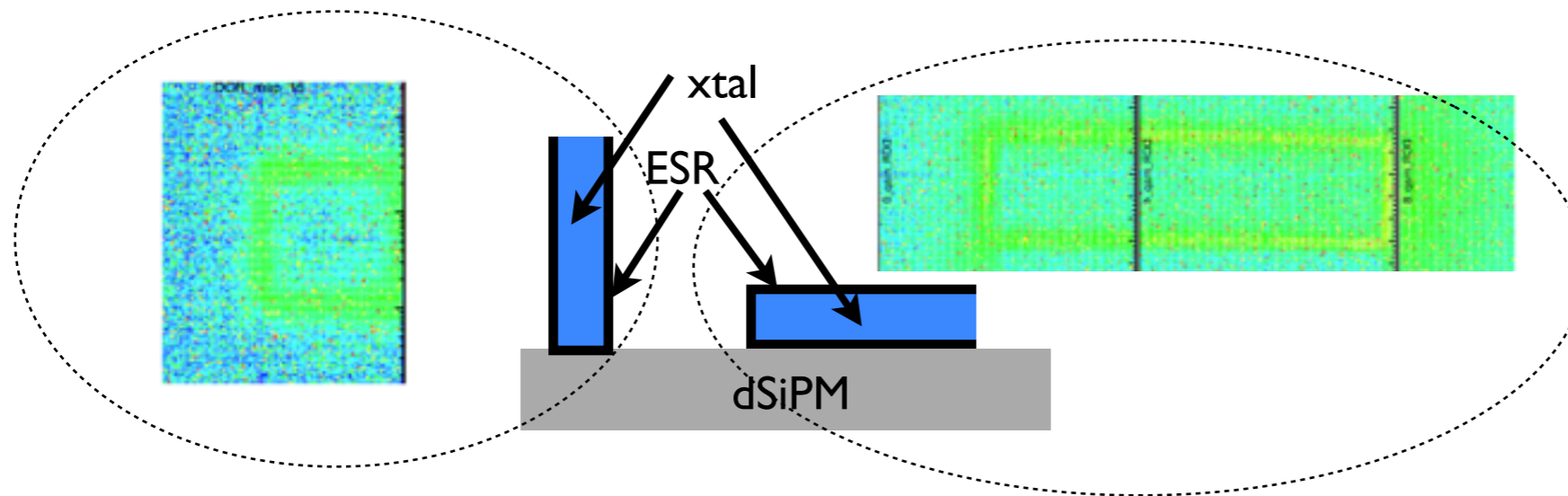


# Low energy contribution

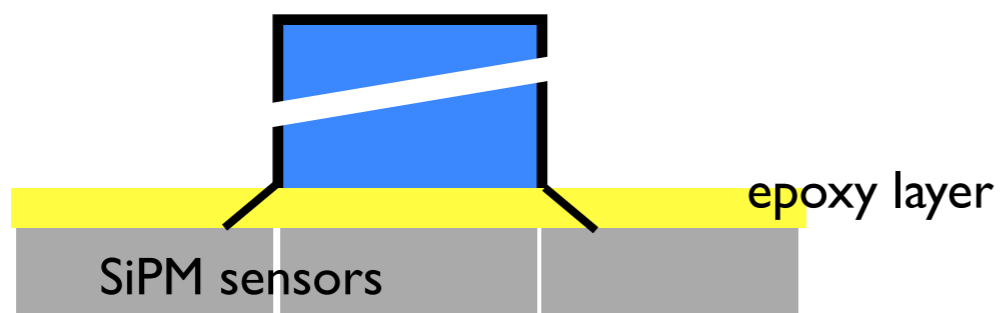
=> There is **LIGHT CORRELATED WITH THE PHOTOPEAK EVENTS** everywhere in the matrix

## Where does it come from?

- **Escaping by the ESR (non-continuous) wrapping**  
by DSiPM (Philips) “dark count maps”  
obtained with crystals on the DSiPM surface and  $^{22}\text{Na}$  source



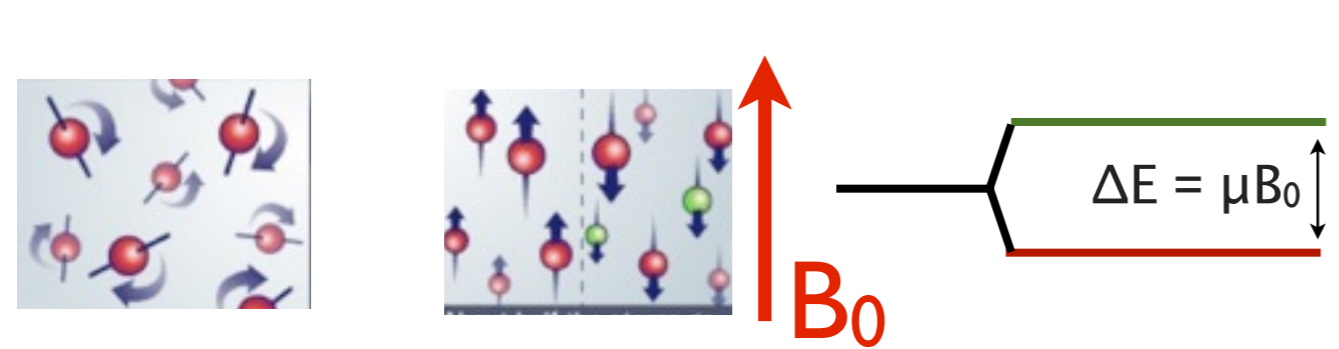
- **SiPM epoxy thickness [also modeled in simulations!]**



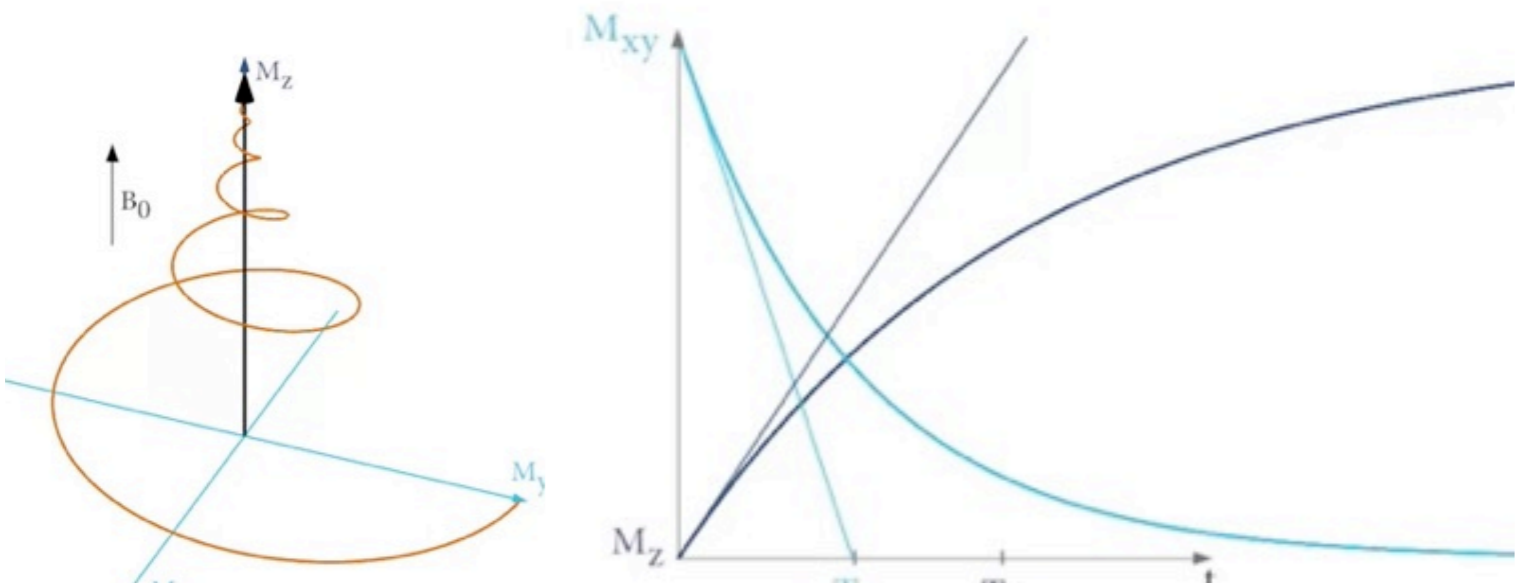
- **cross-talk between SiPM channels of the array (not related with the crystals) ?**

# Magnetic Resonance Imaging (MRI)

- physics basis : **Nuclear Magnetic Resonance (NMR)** : absorption and re-emission of energy by nuclei at their own resonance frequency
- **H** : most abundant element in the body => primary focus of MRI: **H spins**

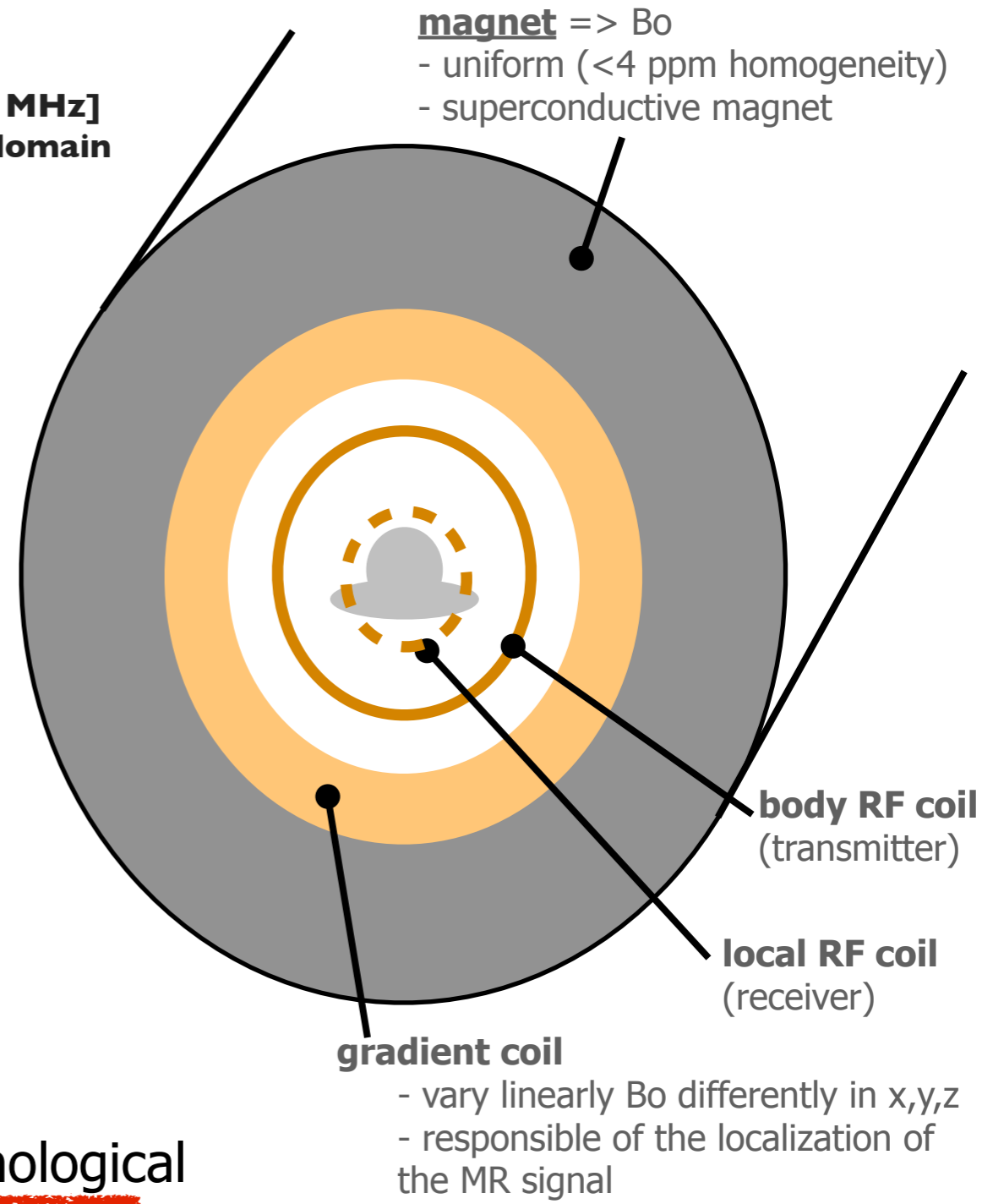


- $B_0$  => net magnetization  $M_0$  (prop. to p density) //  $B_0$
- RF on => Spin Flip => Transverse magnetization
- RF off => relaxation [ $T_1$ ,  $T_2$  time const]



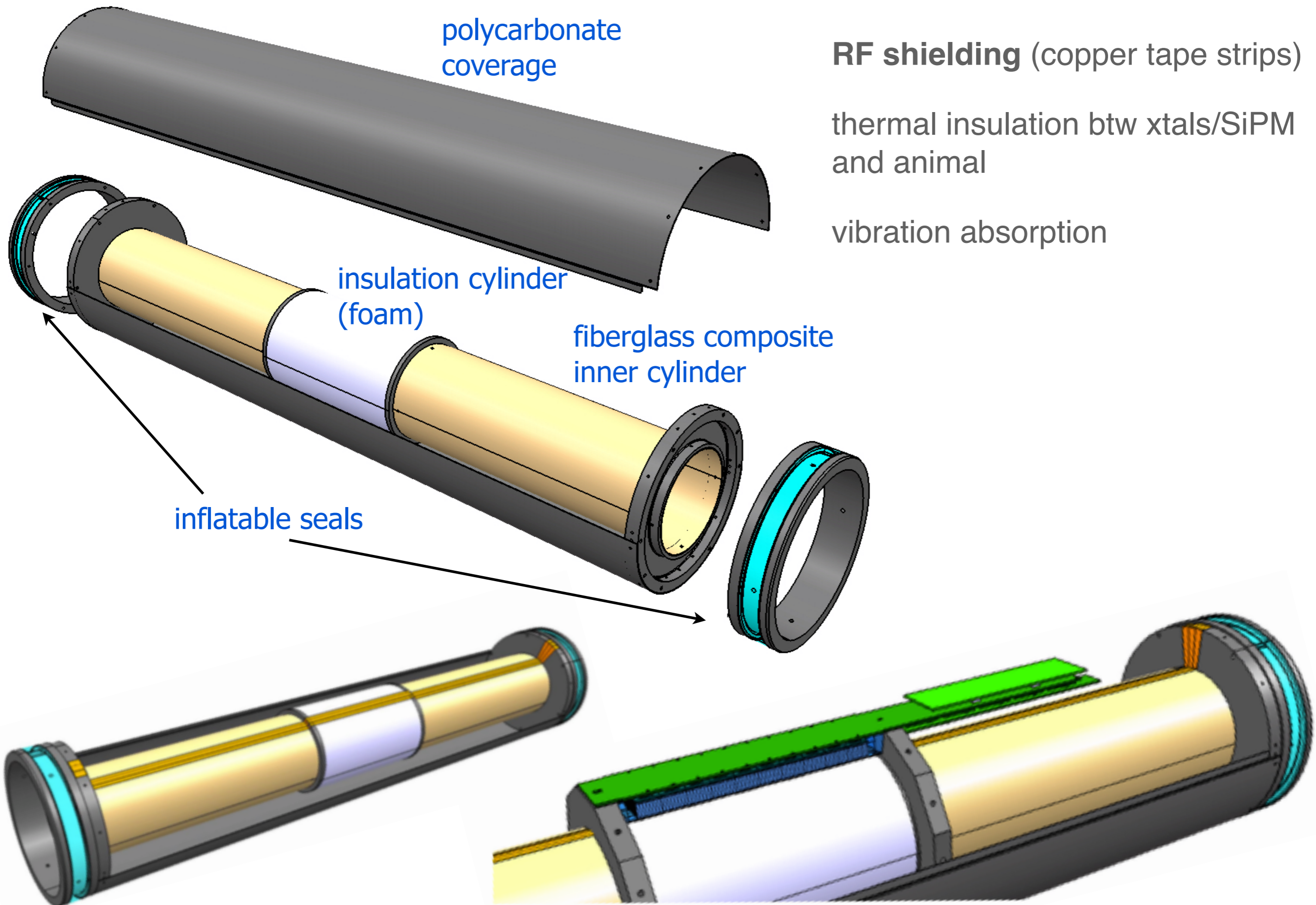
**$M_0, T_1, T_2$  are tissue dependent !!!**

result: map of local transfer magnetization => morphological

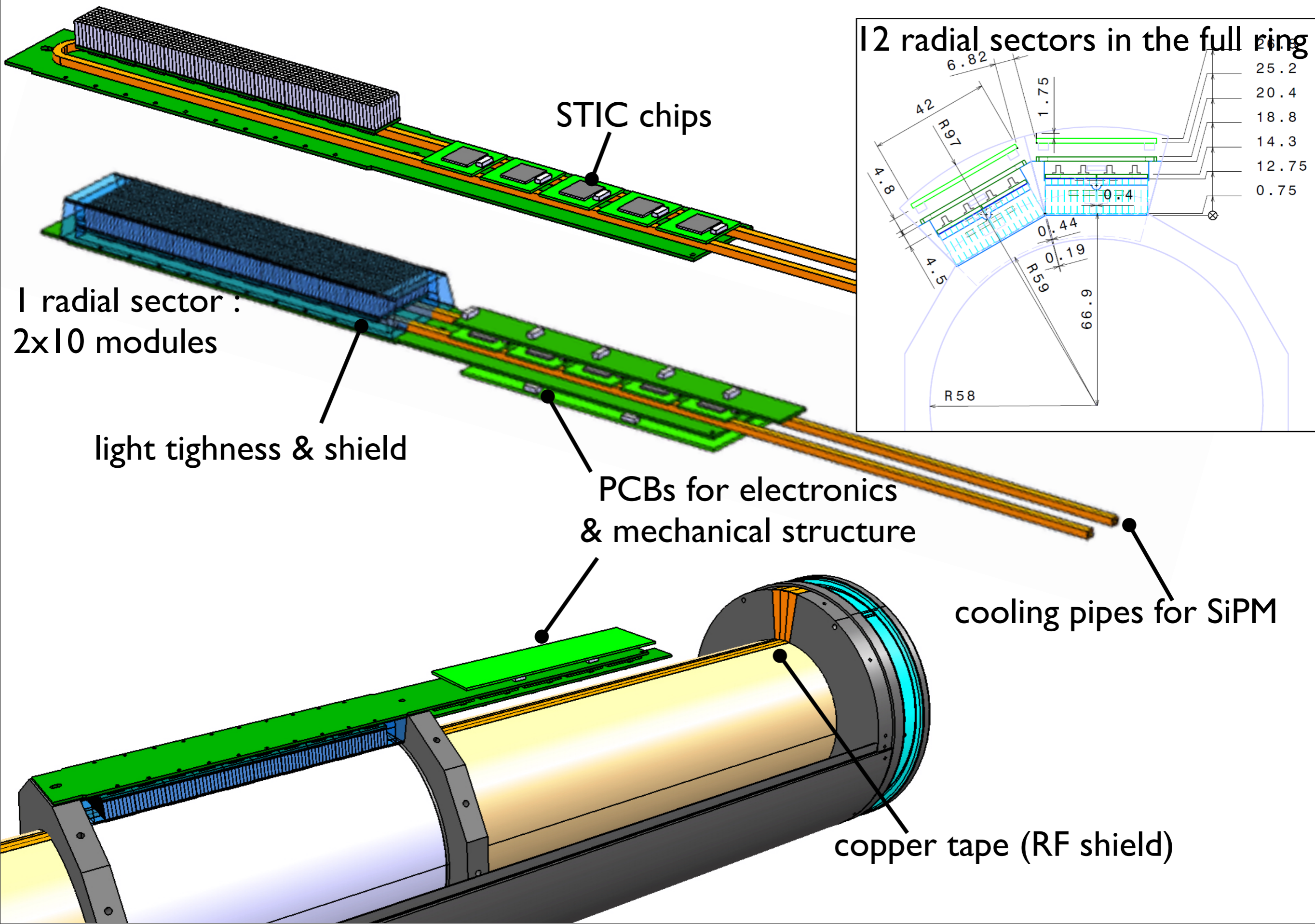




# Mechanics for the insert

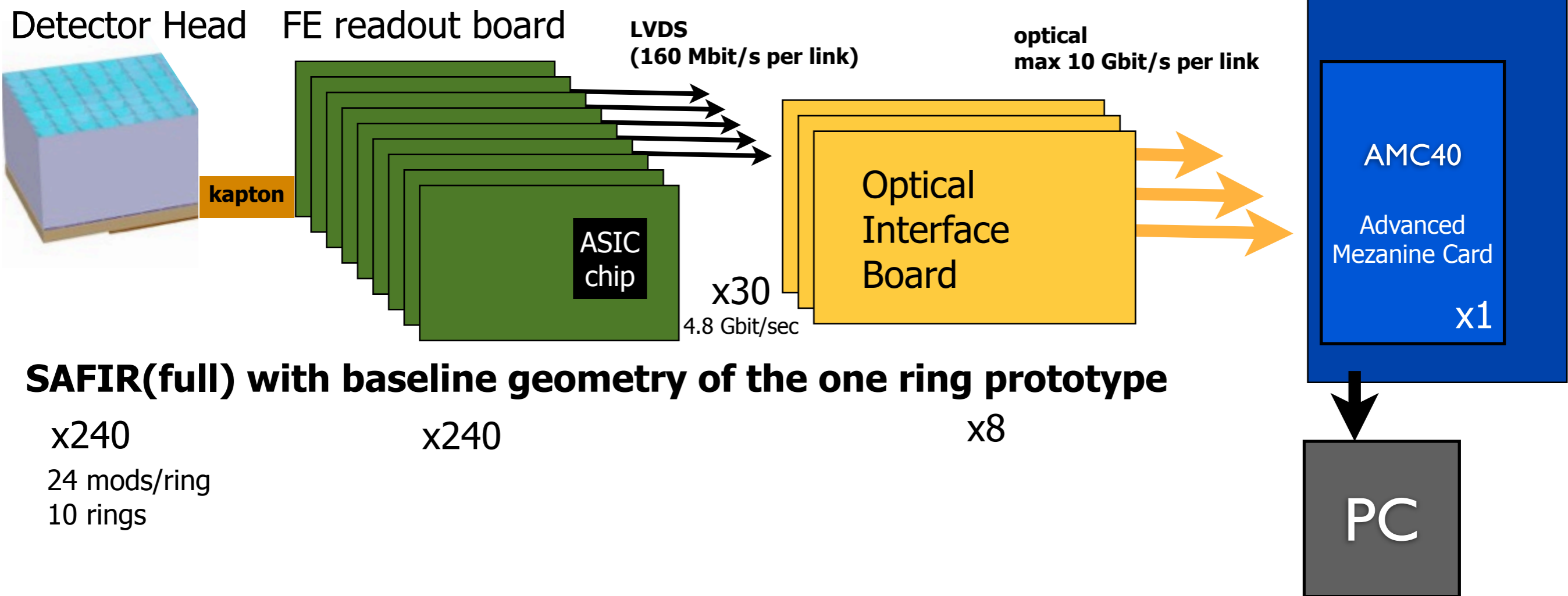


# Extension of the prototype (STIC RO) to a full system

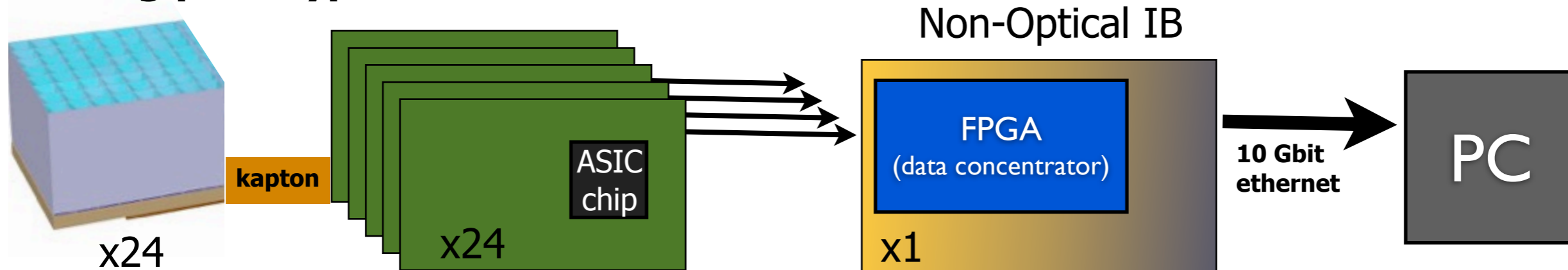


# Readout & DAQ chain

$\mu$ TCA crate  
(micro Telecom Communication Architecture)

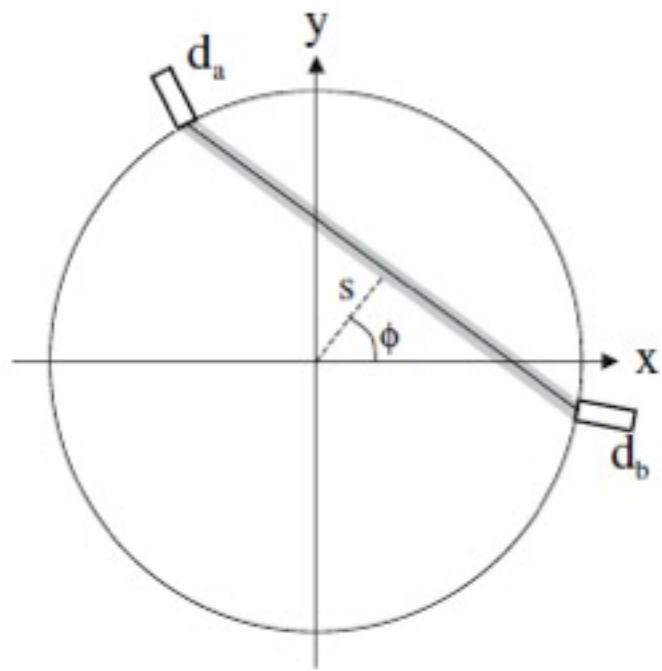


## one ring prototype

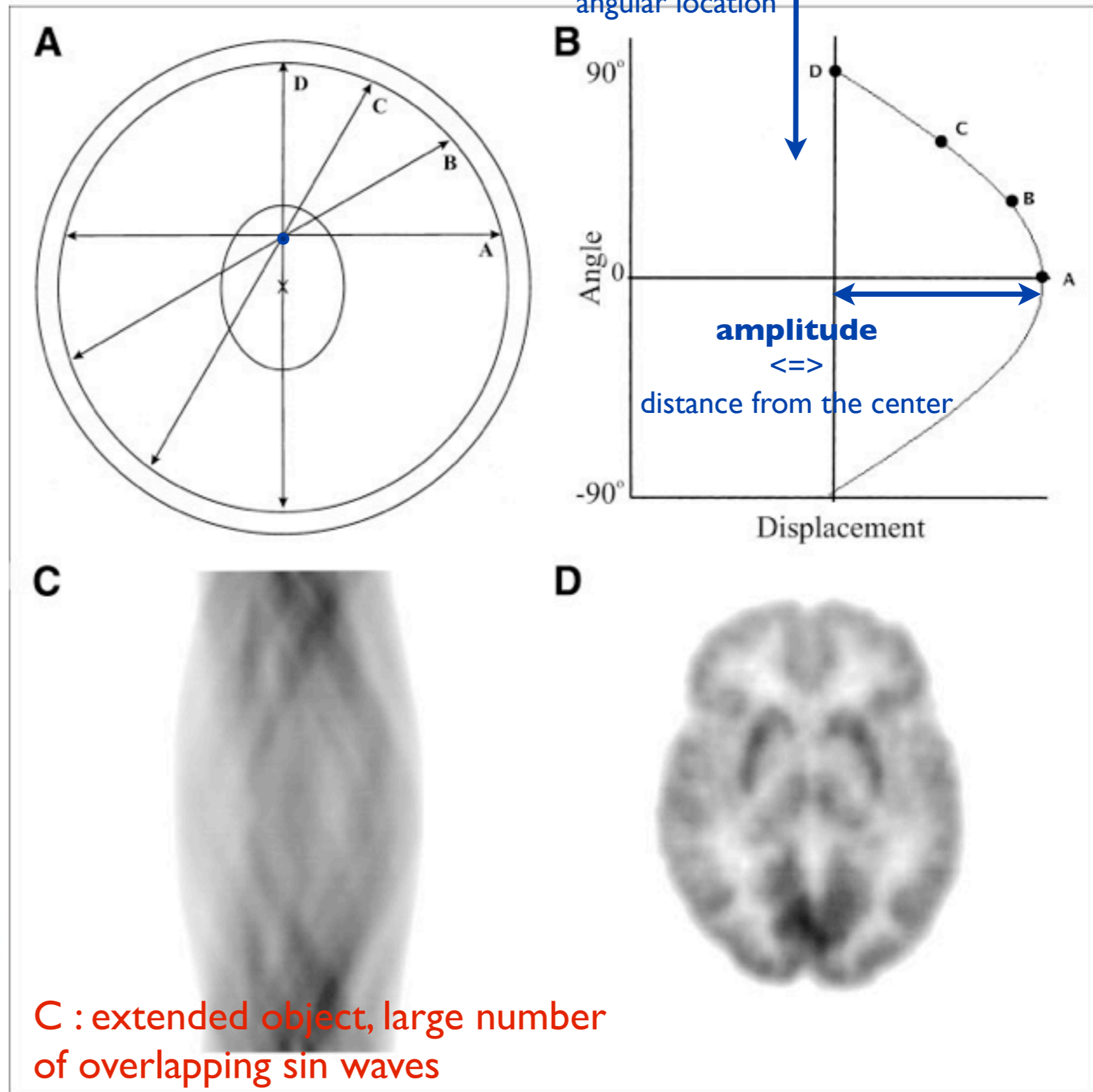


# SINOGRAM

representation in  $(s, \Phi)$  coordinates of all the LOR emitted from a given point in the FOV

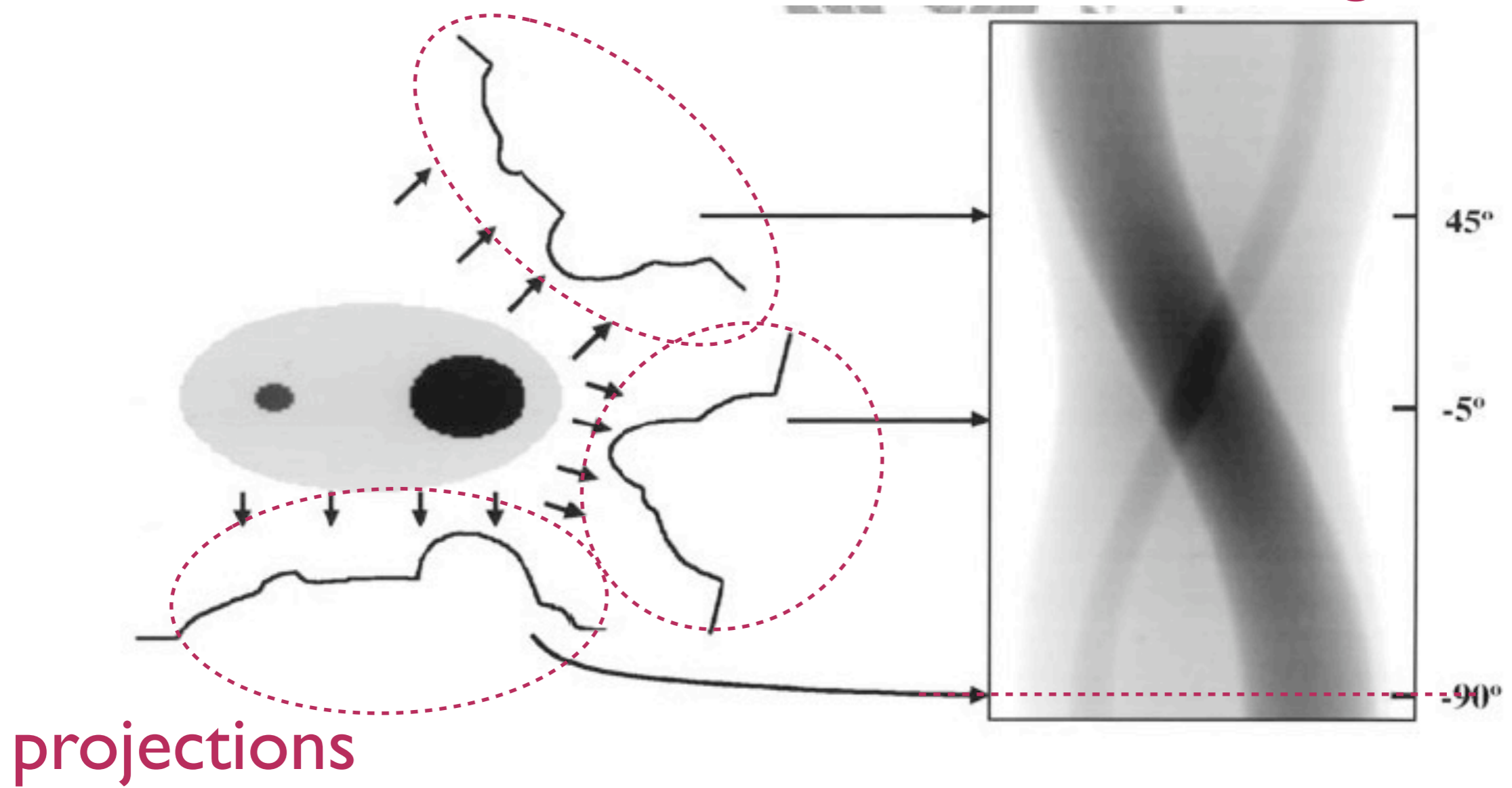


**Figure 4.1.** Schematic representation of a ring scanner. A tube of response between two detectors  $d_a$  and  $d_b$  is represented in grey with the corresponding LOR, which connects the center of the front face of the two detectors. The sinogram variables  $s$  and  $\phi$  define the location and orientation of the LOR.



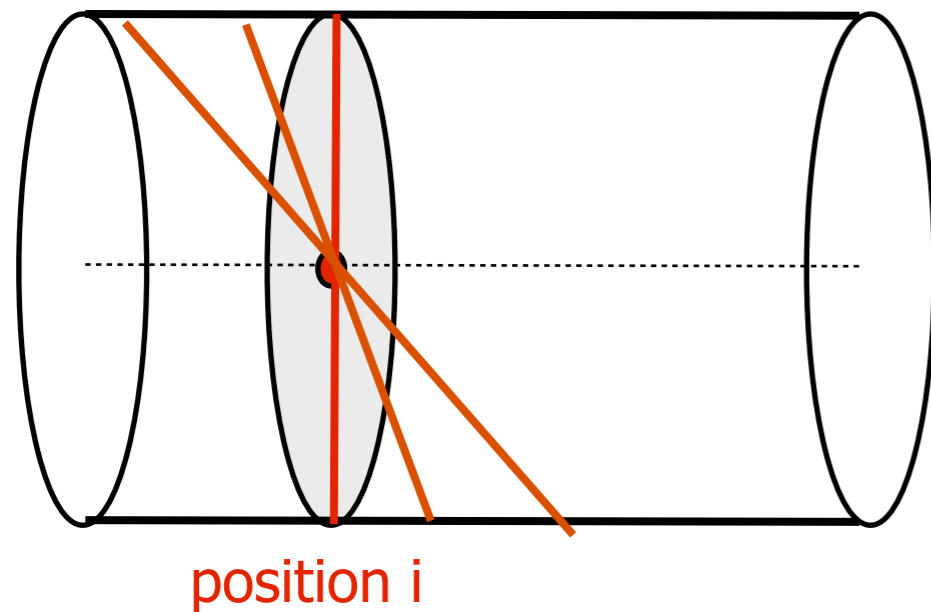
**C : extended object, large number of overlapping sin waves**

sinogram

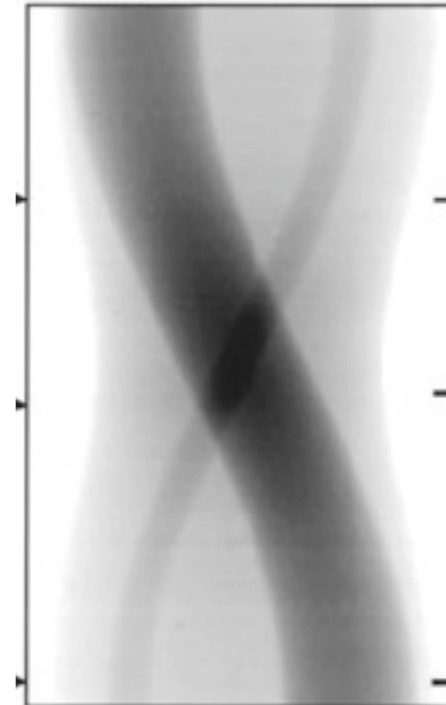
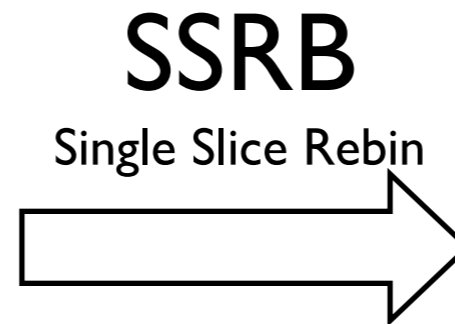


each row in a sinogram is the projection along the angle associated with that row

# Single Slice Rebin [SSRB]



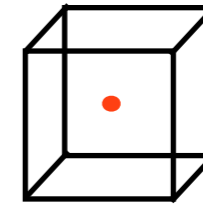
1! sinograms for each i position



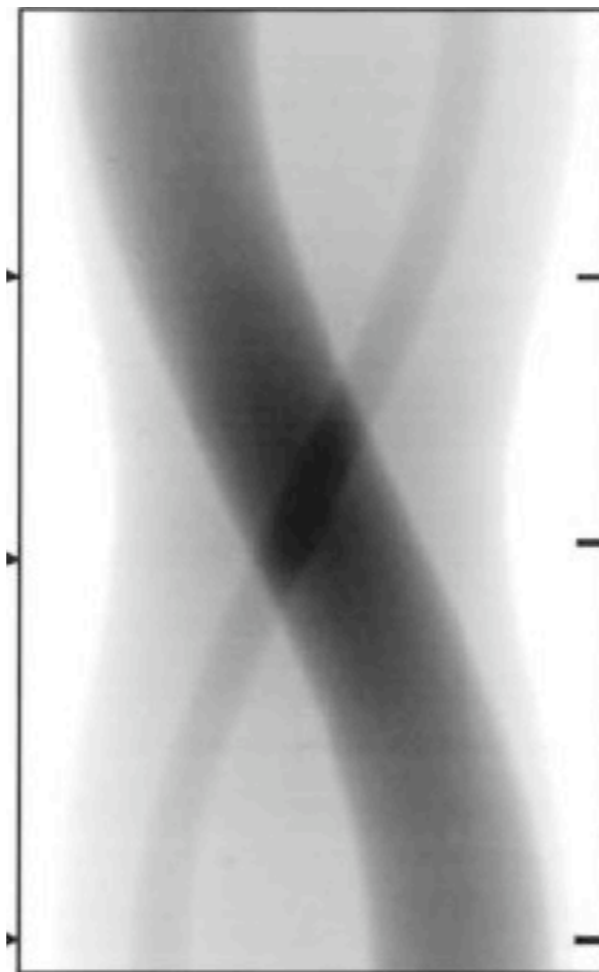
- for each source position (i) :  
the full set of sinograms is rebinned to a single 2D sinogram  
approximation - but acceptable near the center of the scanner and for small apertures

# Spatial resolution - NEMA prescription

- phantom : 1cm<sup>3</sup> acrylic with <sup>22</sup>Na point source at the center
- low activity (Act = 100 kBq)
- moved axially / transaxially (5 mm steps)

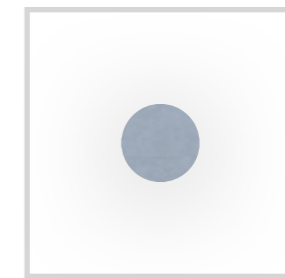
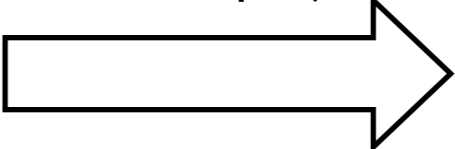


- for each source position (i) :  
a full set of sinograms  
for each axial position  
(accounting for all  
oblique configurations)  
rebinned into one single  
sinogram [SSRB]



1! sinograms for each i position

**FBP**  
Filtered back projection



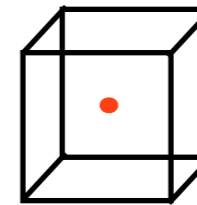
**LINE PROFILE**  
=> Resolutions



# Sensitivity - NEMA prescription

$$\text{Sensitivity} = N_{\text{detected\_coincs}} / N_{\text{annihilations}}$$

- phantom : 1cm<sup>3</sup> acrylic with 22-Na point source at the center
- low activity (Act = 100 kBq)



- moved axially over the full FOV

- for each source position (i) :

10000 **true** coincidences detected

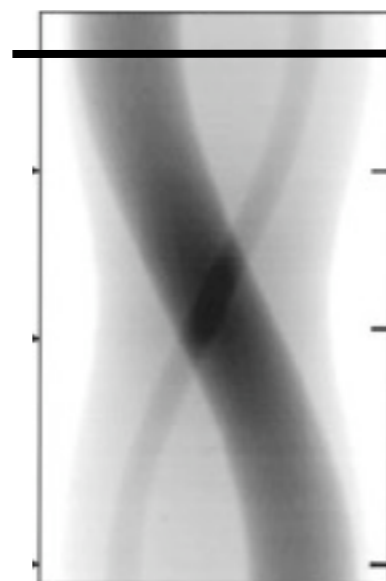
acquisition duration : time  $t_i$

$$N_{\text{annihilations}}(i) = \text{Act} * \text{BR}(=0.90) * t_i$$

- **N\_detected\_coincs** : through reconstructed sinograms

- for each source position (i) :

a full set of sinograms  
for each axial position  
(accounting for all  
oblique configurations)  
rebinned into one single  
sinogram [SSRB]



row j :

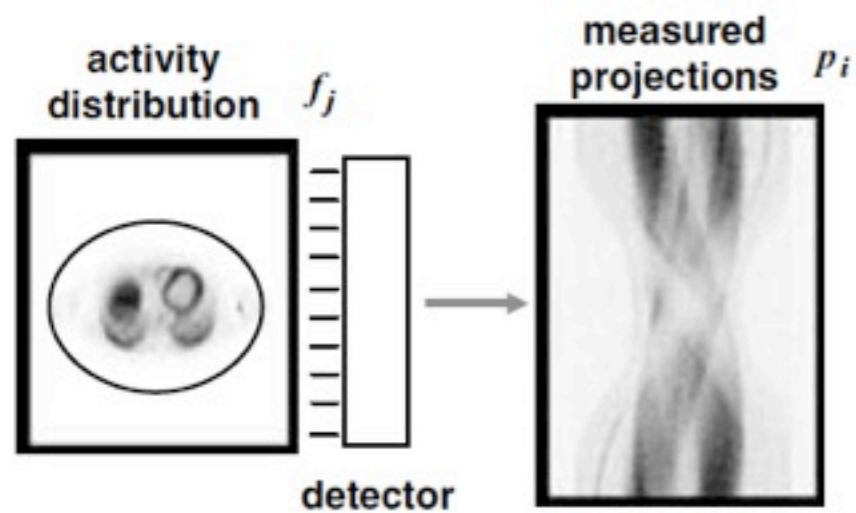
find max

sum counts around max (1cm)

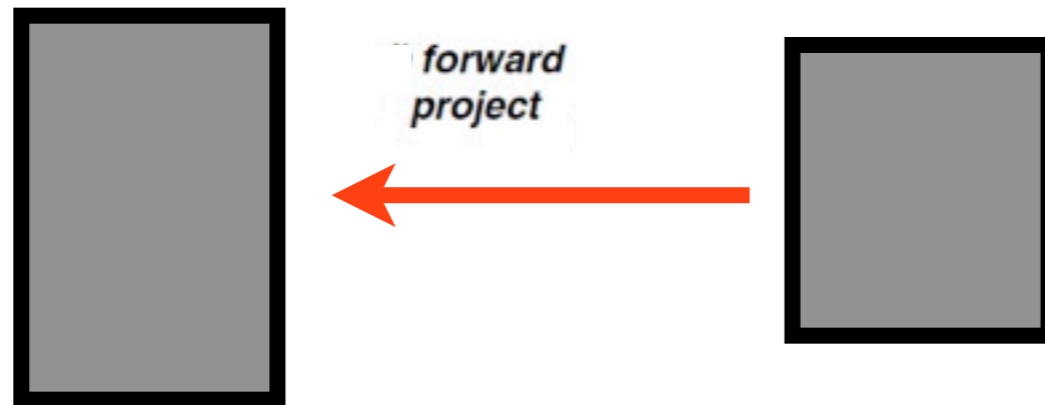
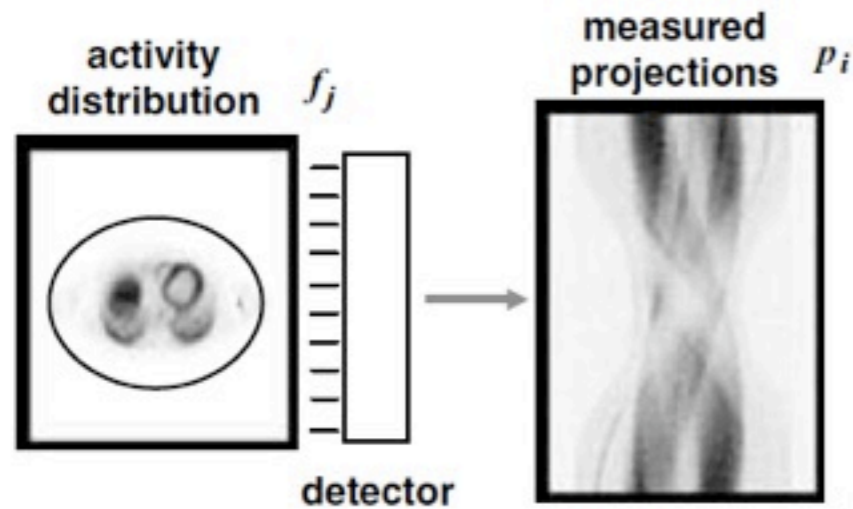
$$N_{\text{detected}}(i) = \text{Sum}_j \text{ counts}$$



# Iterative reconstruction method



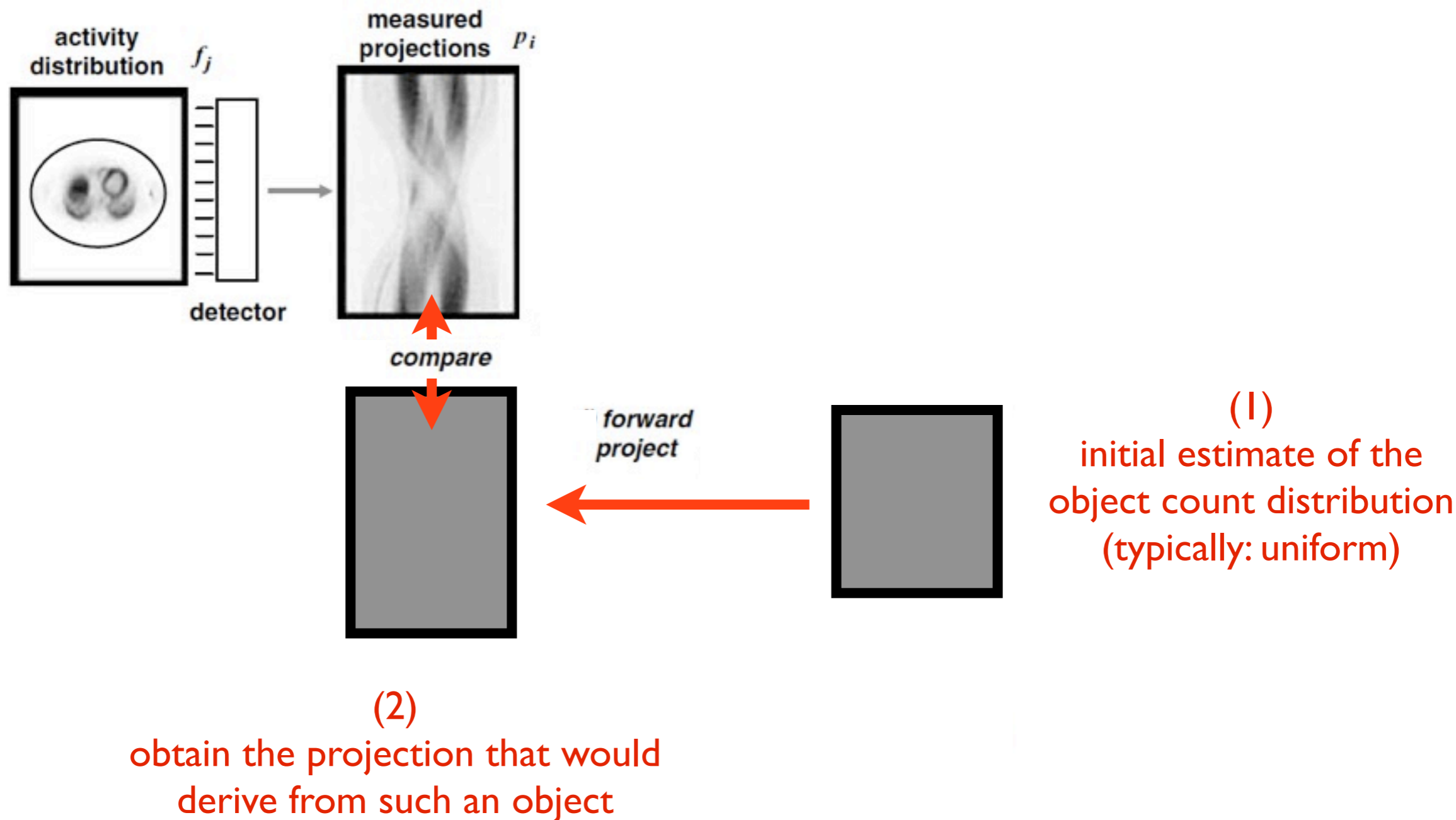
# Iterative reconstruction method



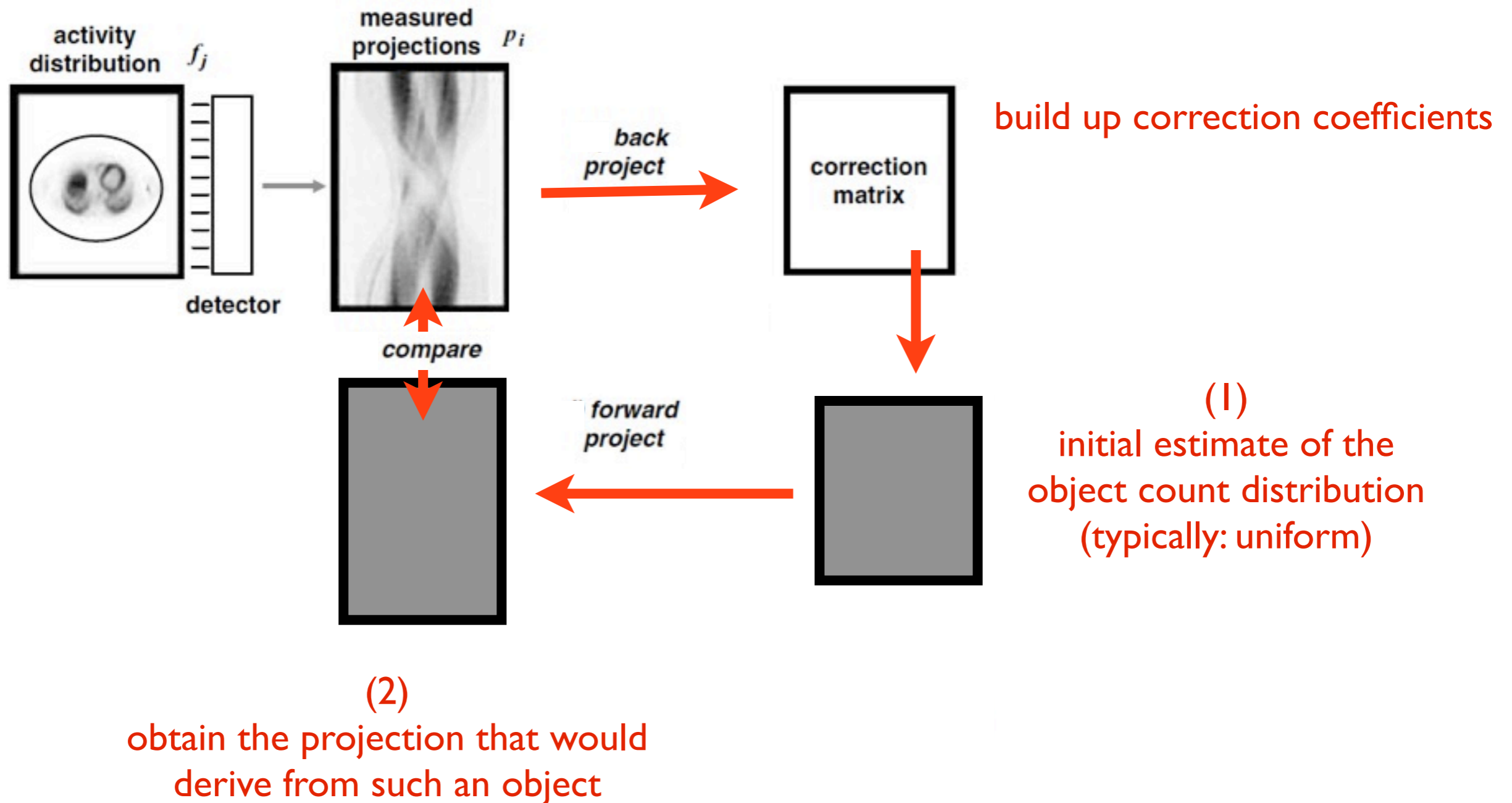
(1)  
initial estimate of the  
object count distribution  
(typically: uniform)

(2)  
obtain the projection that would  
derive from such an object

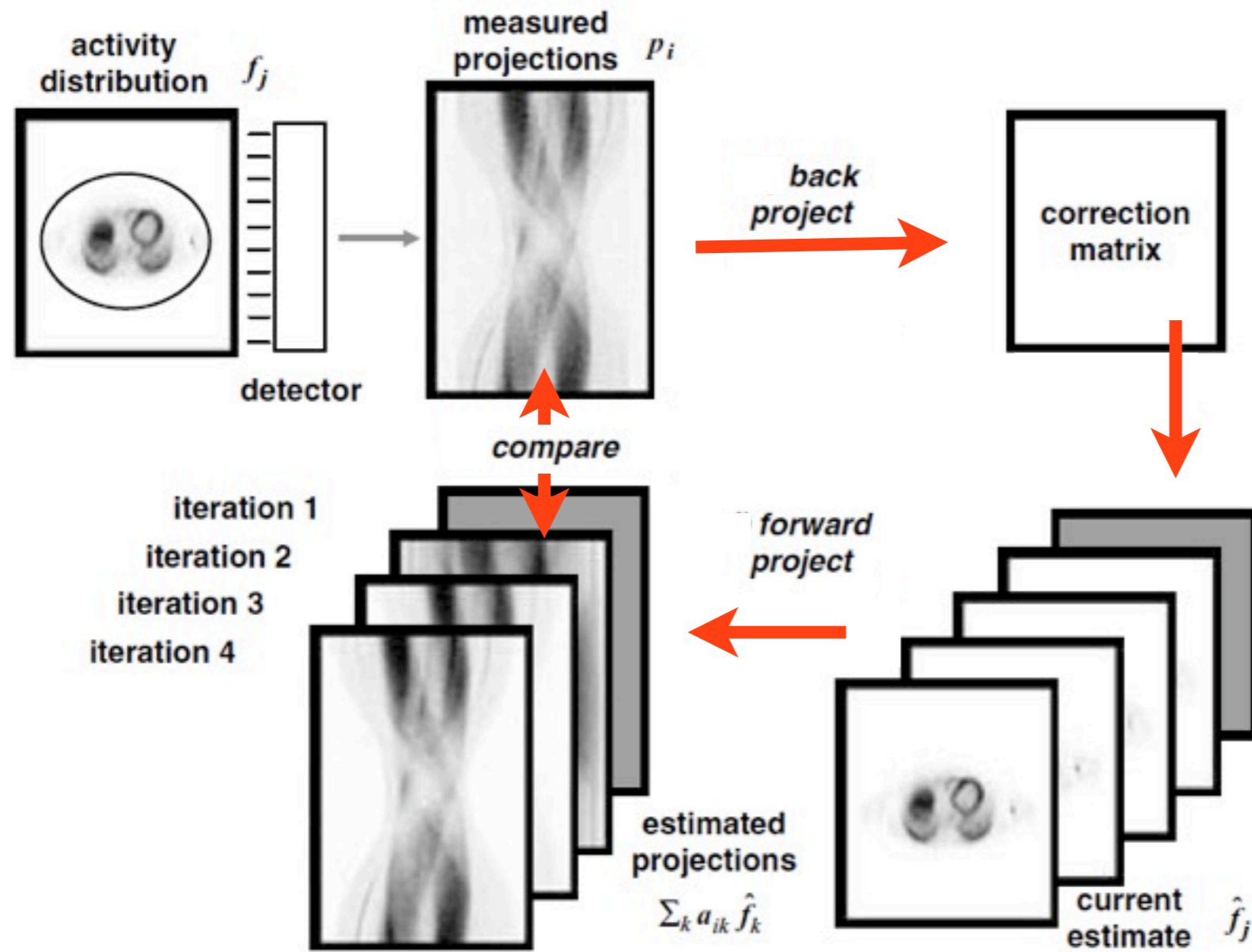
# Iterative reconstruction method



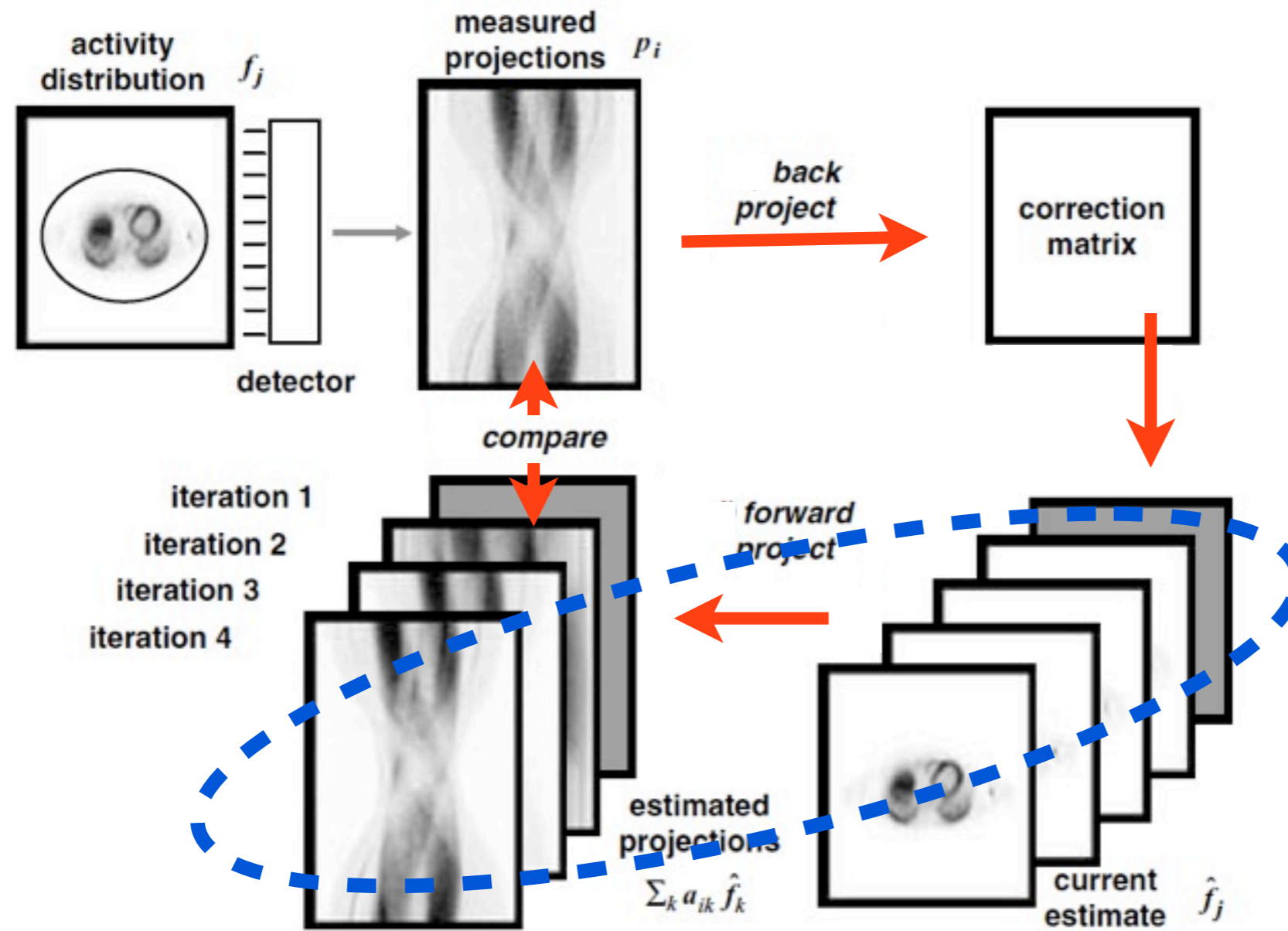
# Iterative reconstruction method



# Iterative reconstruction method



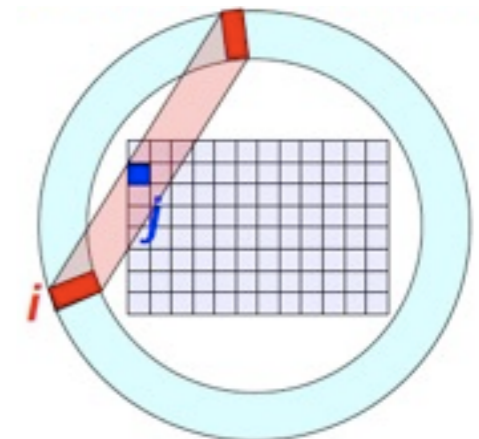
# Iterative reconstruction method



requires a description of the physical model of emission and detection processes :

## SYSTEM MATRIX

$M_{ij}$



probability of the activity in the  $j$ -voxel to be detected by the  $i$ -LOR

includes :

- **geometry** description
- **physics** (e.g. : attenuation)
- **variable fraction of the voxel** contributes to the counts
- ...

out of the many possible iterative methods

**AX-PET** uses **ML-EM**

**Max Likelihood**

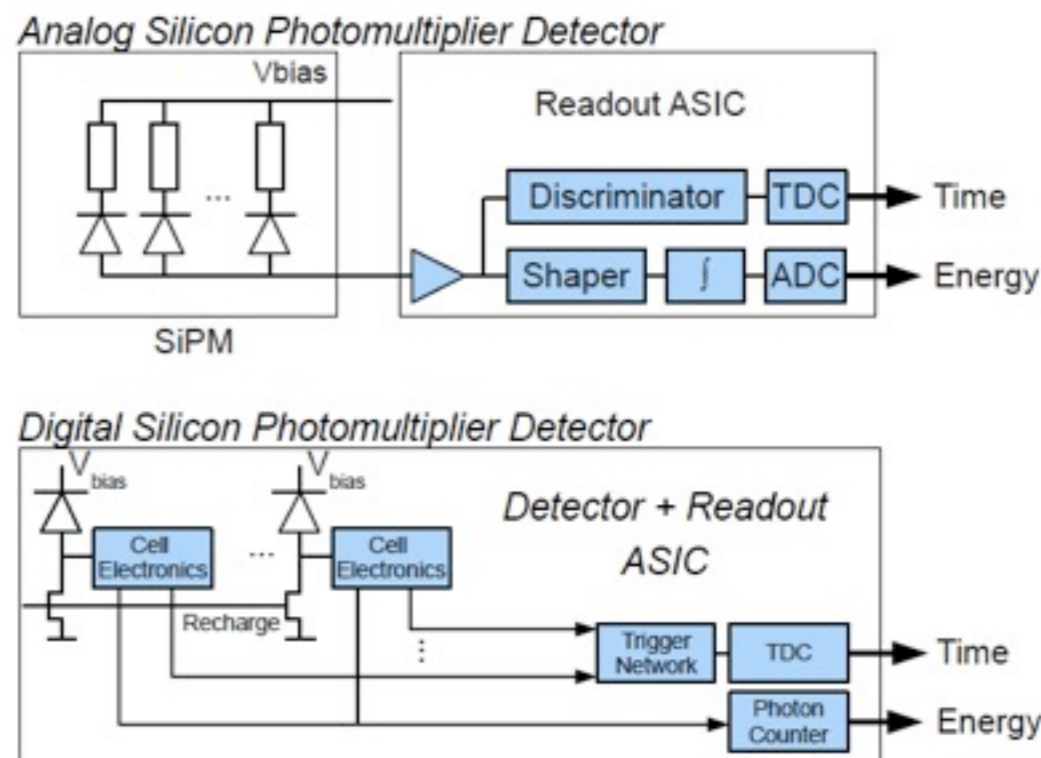
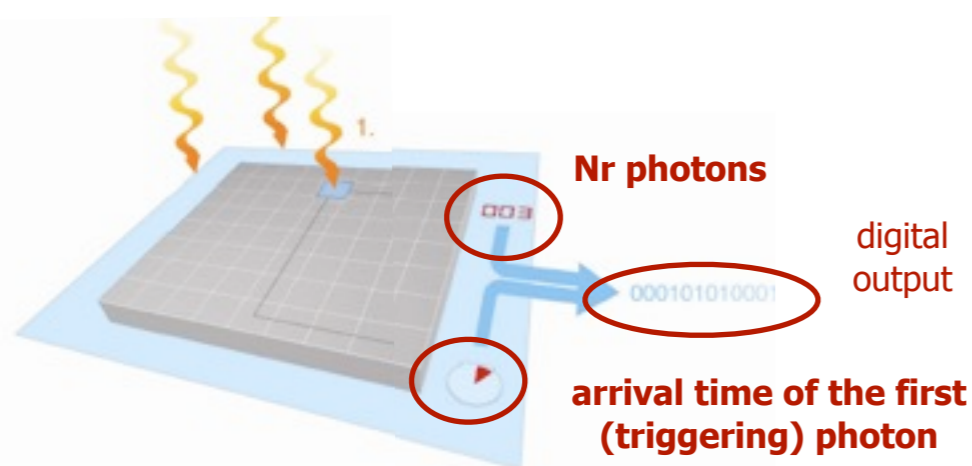
**Expectation Maximization**

two steps per iteration :

- (1) **Expectation step** : form the likelihood of any reconstructed image given the measured data
- (2) **Maximization step** : find the image with the greatest likelihood

# dSiPM : Digital SiPM (Philips)

- fully digital implementation of SiPM
- electronics on the same Si substrate as for the sensor
- on-board TDC (19.5 ps resolution)

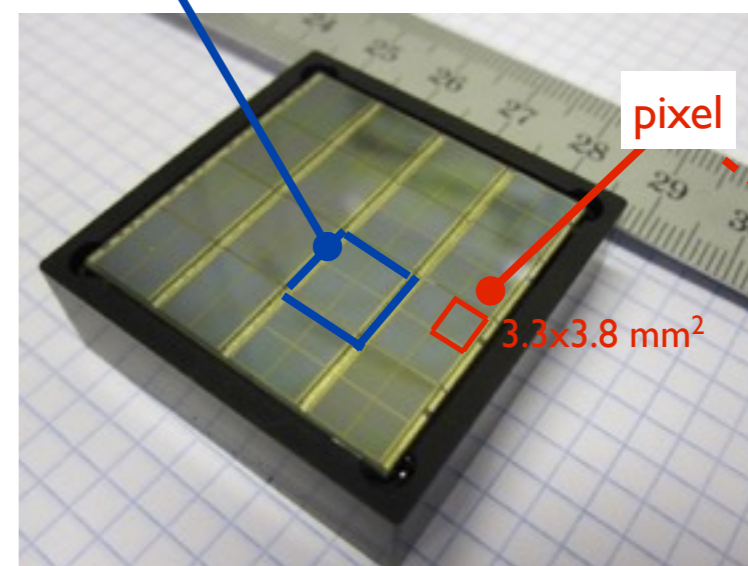


T. Frach

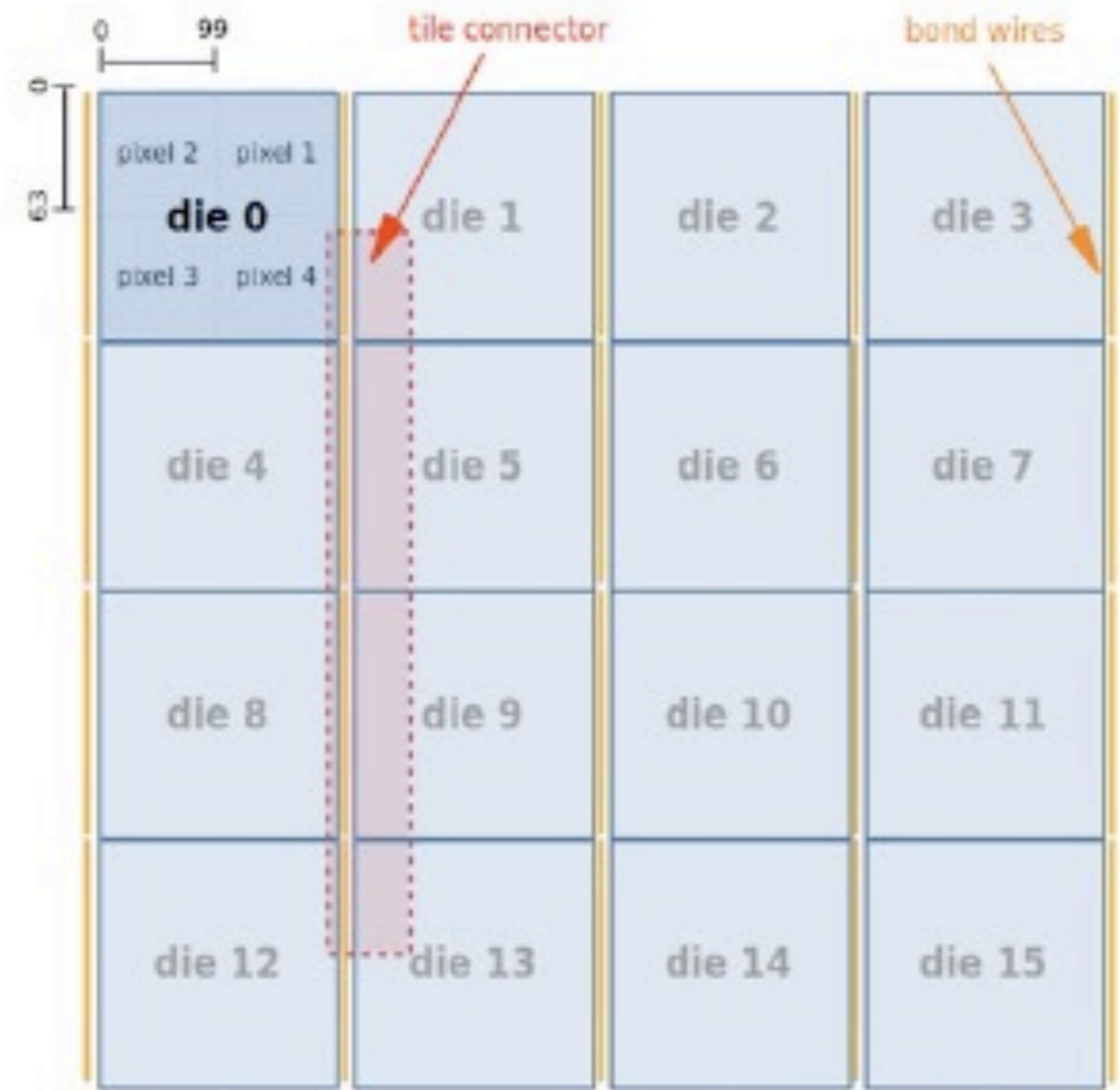
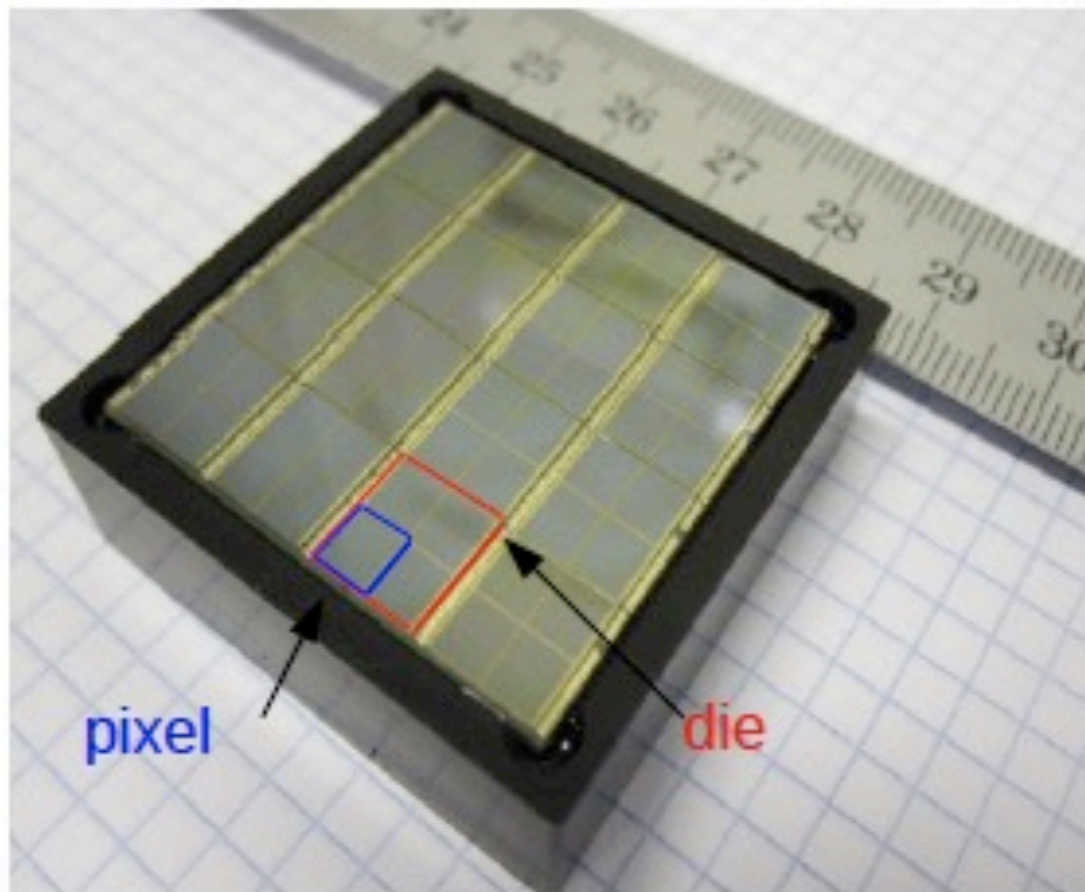
## interest of dSiPM for PET applications :

- **High resolution timing information** => TOF-PET
- **Integration** (bias supply included, amplifier, TDC, photon counter)
- **Compactness**
- Early digitization of the output => **Low noise**
- Digital => **Temperature and gain stability less critical** wrt analogue
- Fast active quenching => no Afterpulses.
- Possibility to disable individual cells => **Reduction in the dark count rate** (but lower PDE)
- MRI compatible

die (=chip) = 4 pixels



- 8x8 pixel matrix
- Each pixel contains 3200 (DLS3200) or 6400 (DLS6400) cells
- Pixel is 3.2 x 3.8 mm<sup>2</sup> ( close to MPPC size)
- Digital device, i.e the output is directly the number of detected photons
- Each event is made of:
  - Die ID
  - timestamp
  - #photons in each pixel composing the die

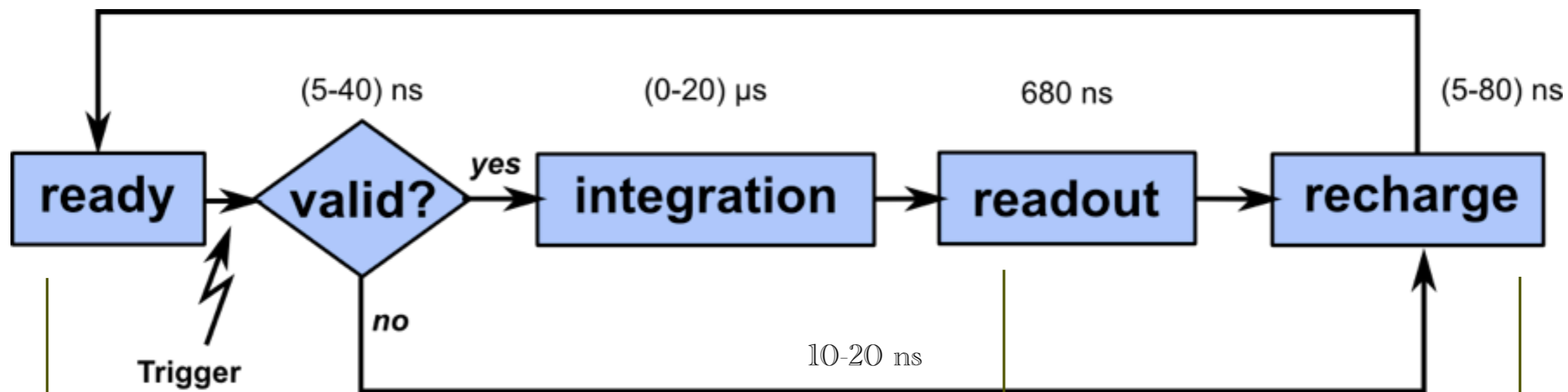


Seen from top  
(glass position)



# Digital Silicon Photomultiplier (D-SiPM)

## pixel (i.e. 3200/6400 diodes) state machine :



Trigger  
(1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>  
photon)

↳ Timestamp

higher **trigger** level: better control of the system dead time but loss of time resolution

10-20 ns

**READOUT:** proceeds line by line - The nr photons detected in a line is added to the photons accumulator  
 - While reading out one line, the preceding one is recharged  
 Sensor is still sensitive during readout => ~1/2 readout time still contributes to the integration time

### READY :

all diodes charged above breakdown  
 recharge transistors open

### RECHARGE / RESET :

global pixel recharge  
 TDC reset

If the trigger is validated, the full readout starts -  $\Sigma < 1 \mu\text{s}$  => Rates ~ MHz can be sustained

Every non-validated trigger leads to the recharging of all cells. **Without cooling, the device can loose efficiency/availability.**

# Digital vs Analogue SiPM

SiPM : intrinsically already a "digital" device

**PHILIPS**  
Digital SiPM – New Type of Silicon Photomultiplier

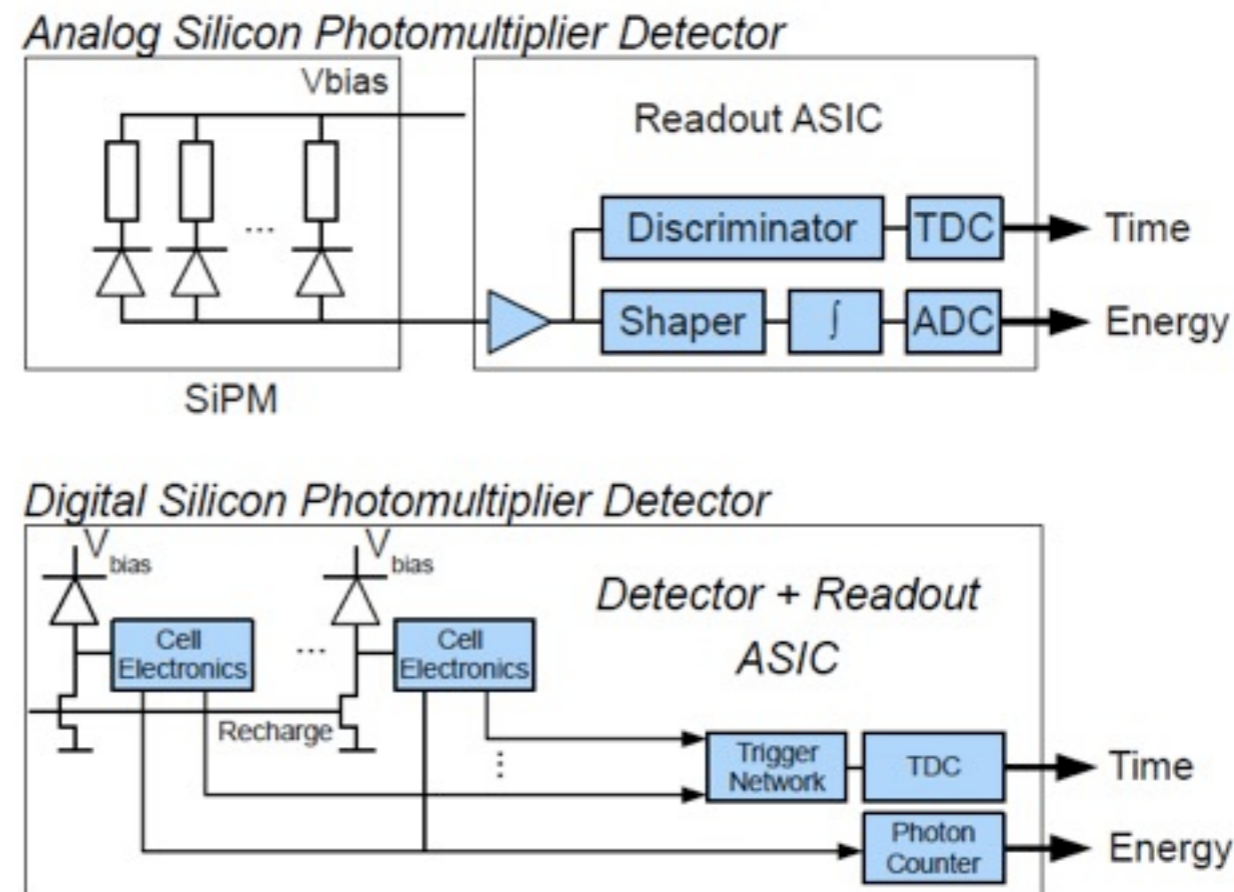
**Analog SiPM**

• 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



## Advantages of digital vs analogue:

- integration (bias supply, amplifier, TDC, photon counter)
- compactness
- (very good timing resolution)
- early digitization of the cell output => low noise
- digital => Temp and Gain stability less critical
- fast active quenching => no afterpulses
- possibility to deactivate individual noisy cells => low dark count rate

## Shared limitations digital / analogue :

- limited nr of cells => saturation
- high dark count rates

## Drawbacks:

- cooling advisable / needed
- long readout time ( $\sim 1 \mu\text{s}$ ) over a quite large detector surface ( $8 \times 8 \text{ mm}^2$ ) => deadtime / availability issues
- lack of flexibility: readout functionality is designed into the sensor; in case of mismatch with the needs expensive FPGA/sensor modifications required