Different detector concepts for several imaging scenario: from hadron-therapy monitoring to clinical imaging.

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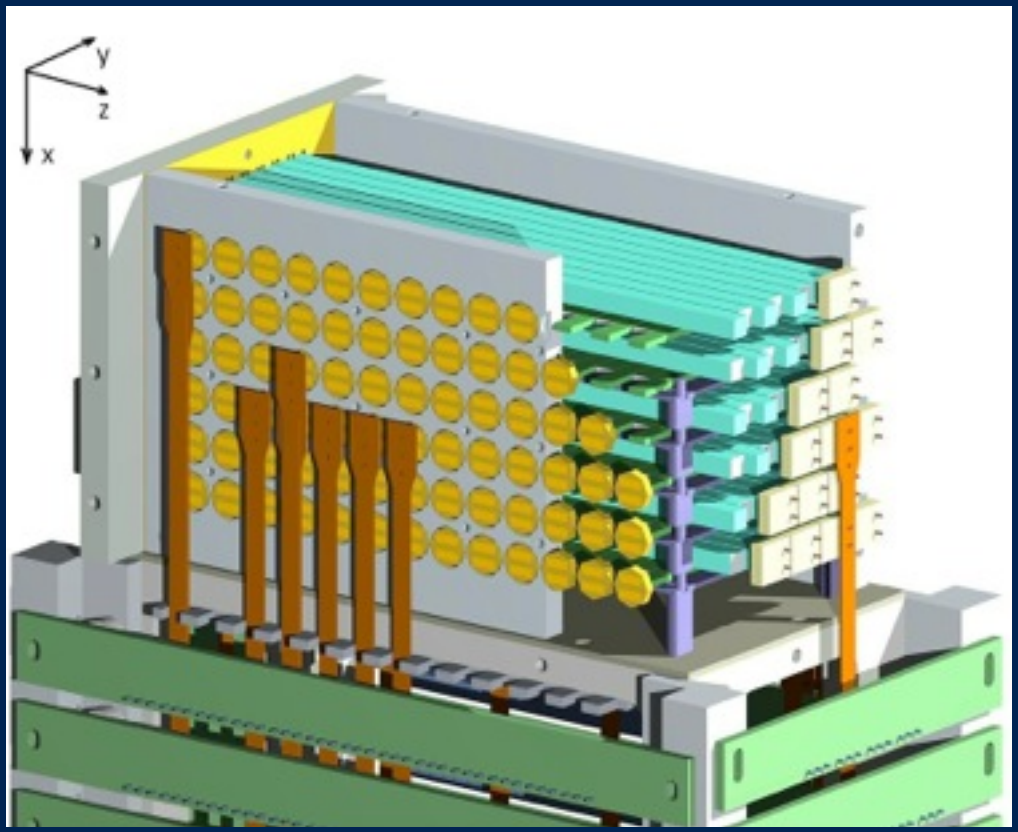
AX-PET

- The concept of a novel PET detector with axial crystals
- New approach to Sensitivity enhance AX-PET
- The modeling of AX-PET
- Towards a Full ring brain scanner

HADRON-THERAPY MONITORING

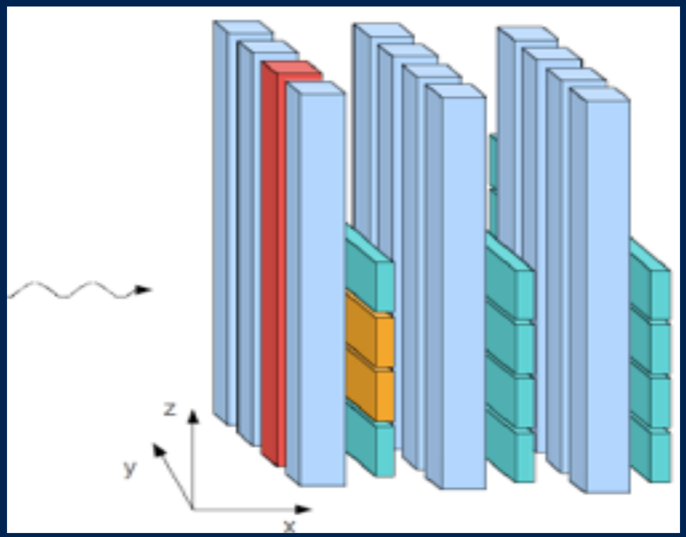
- The verification in HT treatments
- Compton Telescope based on monolithic LaBr3 for Prompt gamma imaging
- PET monitoring: the AX-PET case.

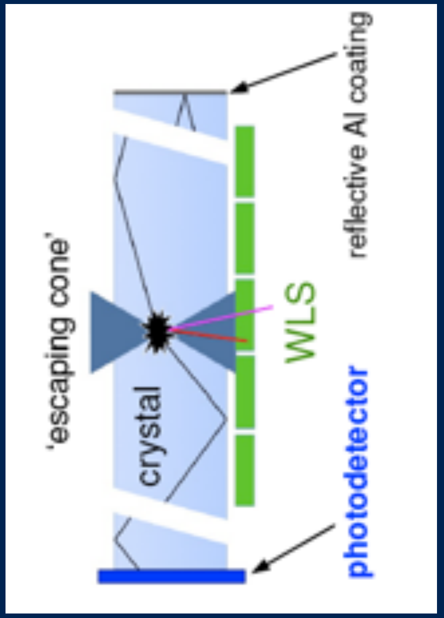
AX-PET: the concept



- Axially oriented crystals: 3x3 mm^2 section, 100 mm long arranged in a 6x8 matrix.
- Wavelength Shifter strip array interleaved to each crystal layer to recover axial coordinate.
- Individual read-out by SiPM of LYSO and WLS.

Once the gamma interacts in the LYSO:
■ photons inside cone of total reflection in LYSO are detected by MPPC;
■ photons outside cone of total reflection in LYSO absorbed by WLS.

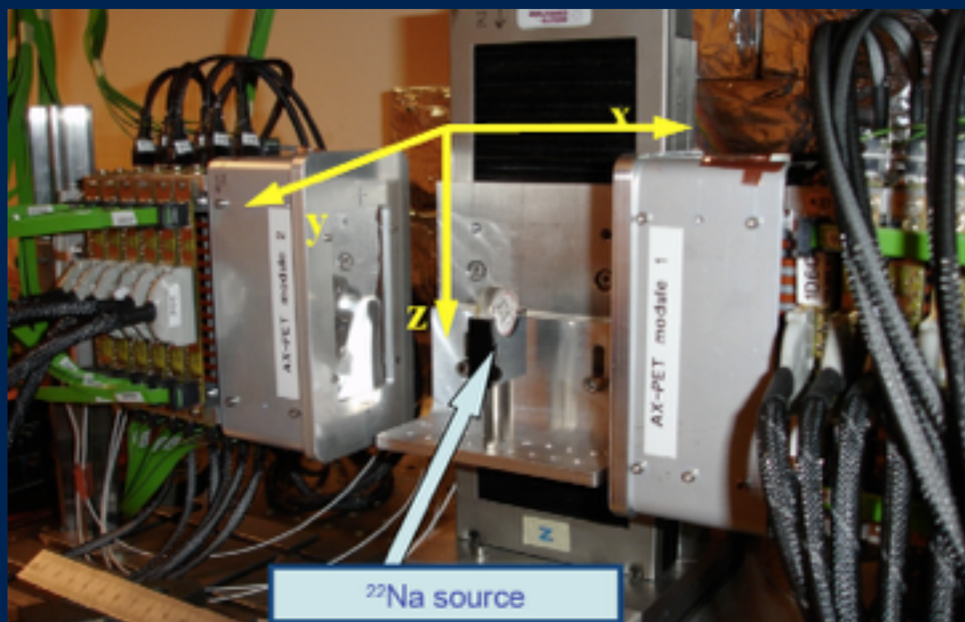




The rationale of AX-PET

Individual read-out + layered arrangement	Decoupling of spatial resolution from sensitivity
WLS + LYSO individually read-out	Fully scalable design to be adjusted to the desired application
3D localization of the gamma interaction	Tracking of Triple events
SiPM+WLS+LYSO	MRI compatible and TOF potential

AX-PET demonstrator

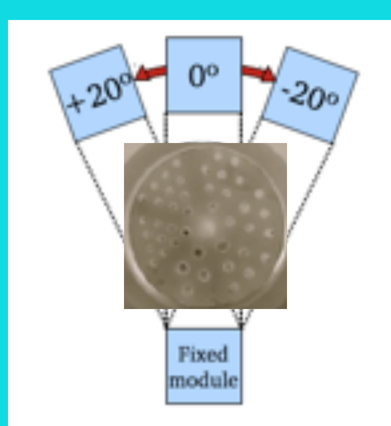


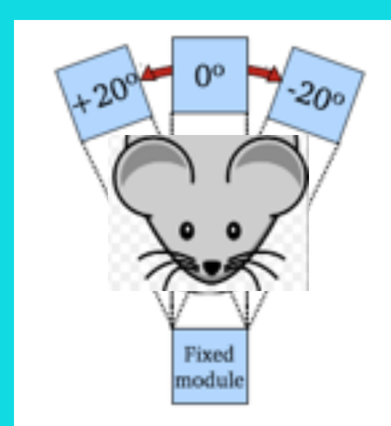
Two modules fully assembled and characterized

Few numbers:
$FWHM_{x,y}$ = 2.03 mm $FWHM_{z}$=1.79 mm $FWHM_{E,511}$ = 11.7%

Coincidence formation:
- LL (~50 keV) at each LYSO crystal
- HL,HHL (400,600 keV) on the LYSO sum per module
- Coincidence window ~40 ns

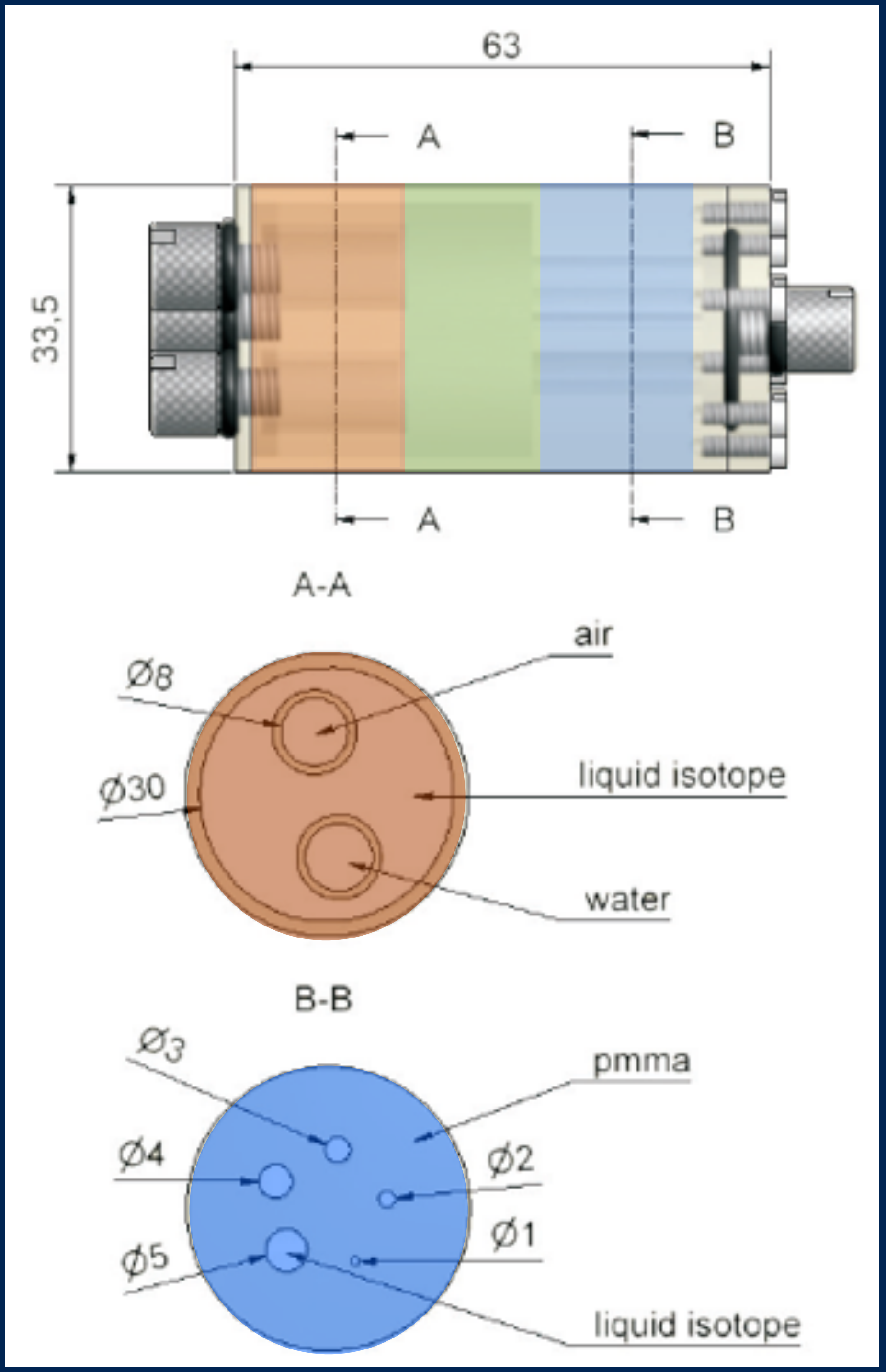
AX-PET on tour
- AAA for phantom imaging
- ETH radio-pharmaceutical lab for phantom and small animal

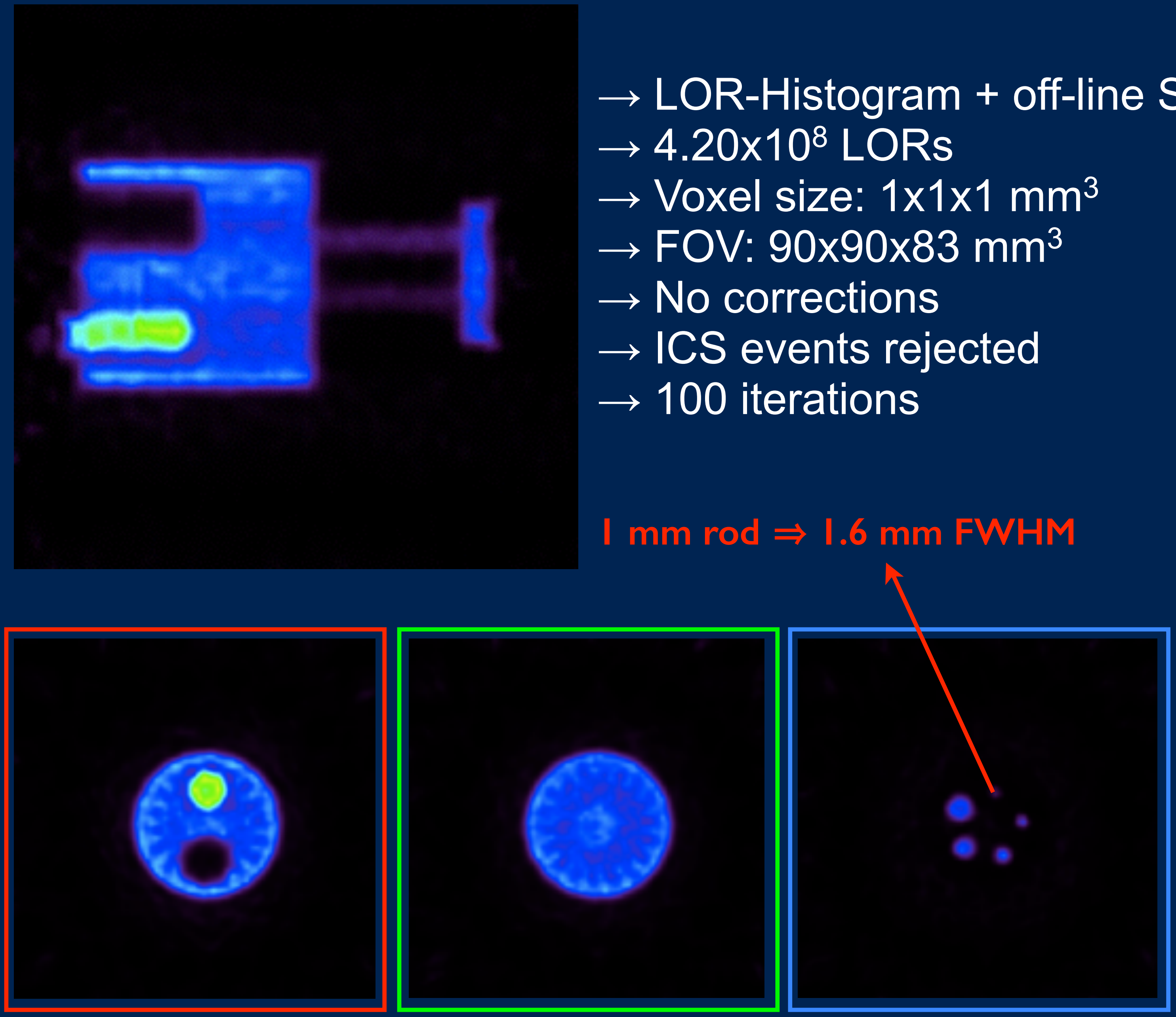




AX-PET proof of concept

QRM-MicroPET-IQ manufactured by QRM





→ LOR-Histogram + off-line SM
→ 4.20×10^8 LORs
→ Voxel size: 1x1x1 mm^3
→ FOV: 90x90x83 mm^3
→ No corrections
→ ICS events rejected
→ 100 iterations

1 mm rod ⇒ 1.6 mm FWHM

Sensitivity enhance through Triple inclusion

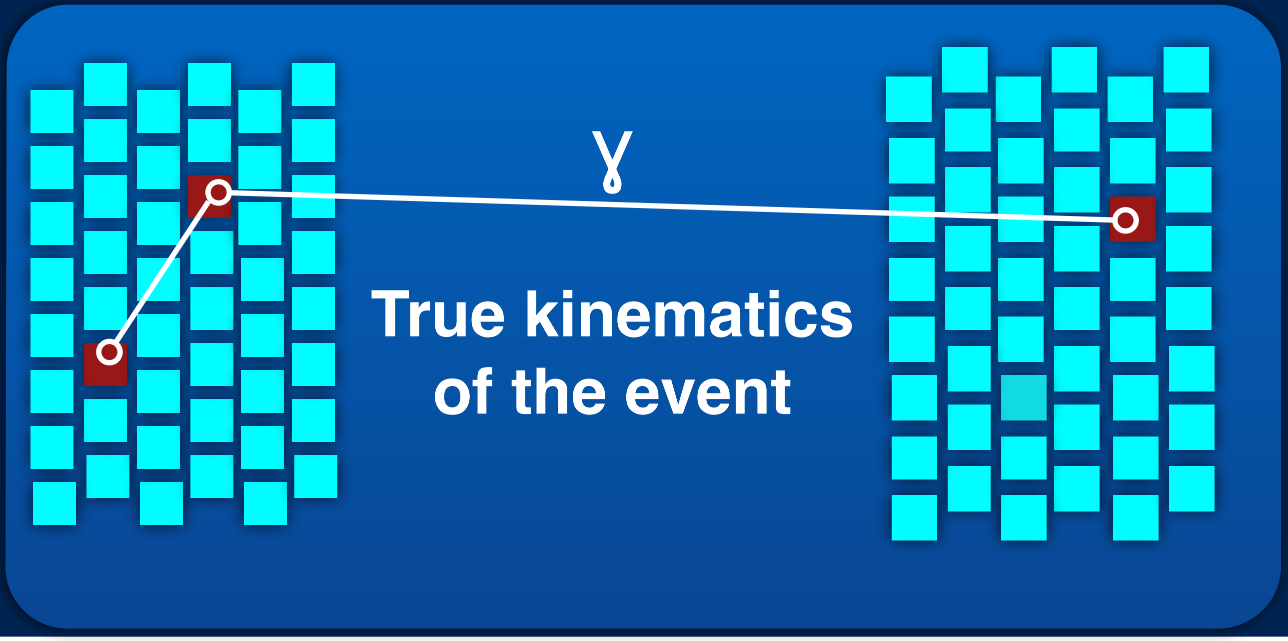
Sensitivity is crucial in PET imaging:

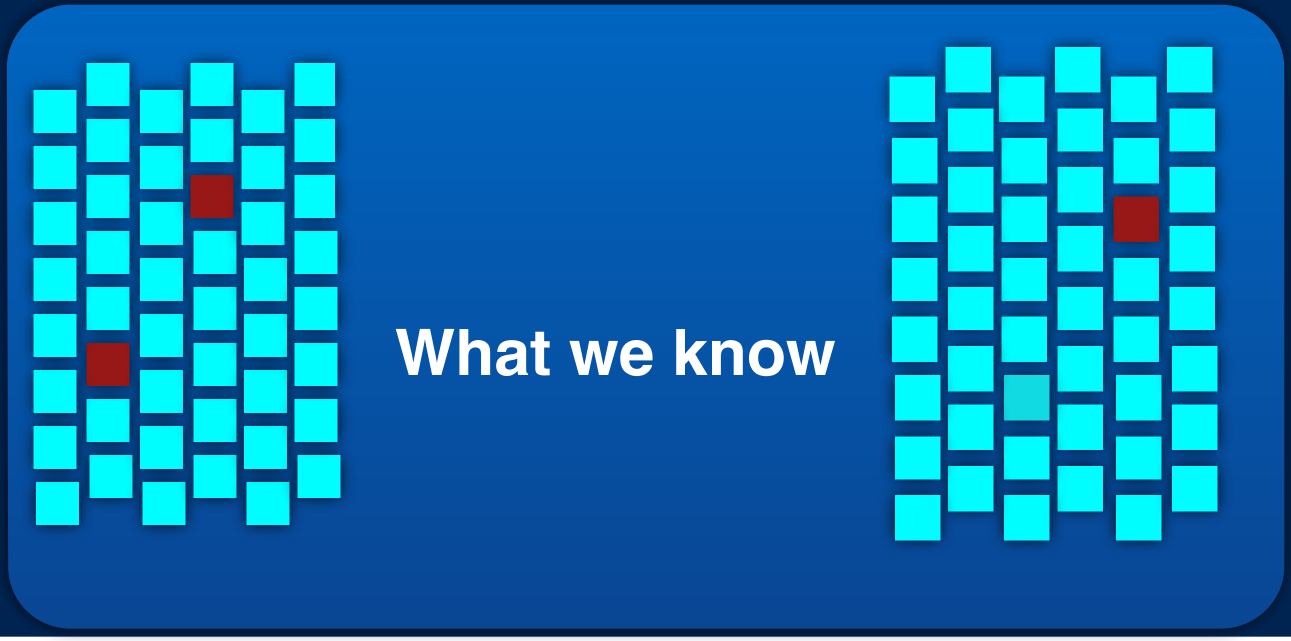
→ Reduction of the dose to the patient

→ Noise reduction in reconstructed images

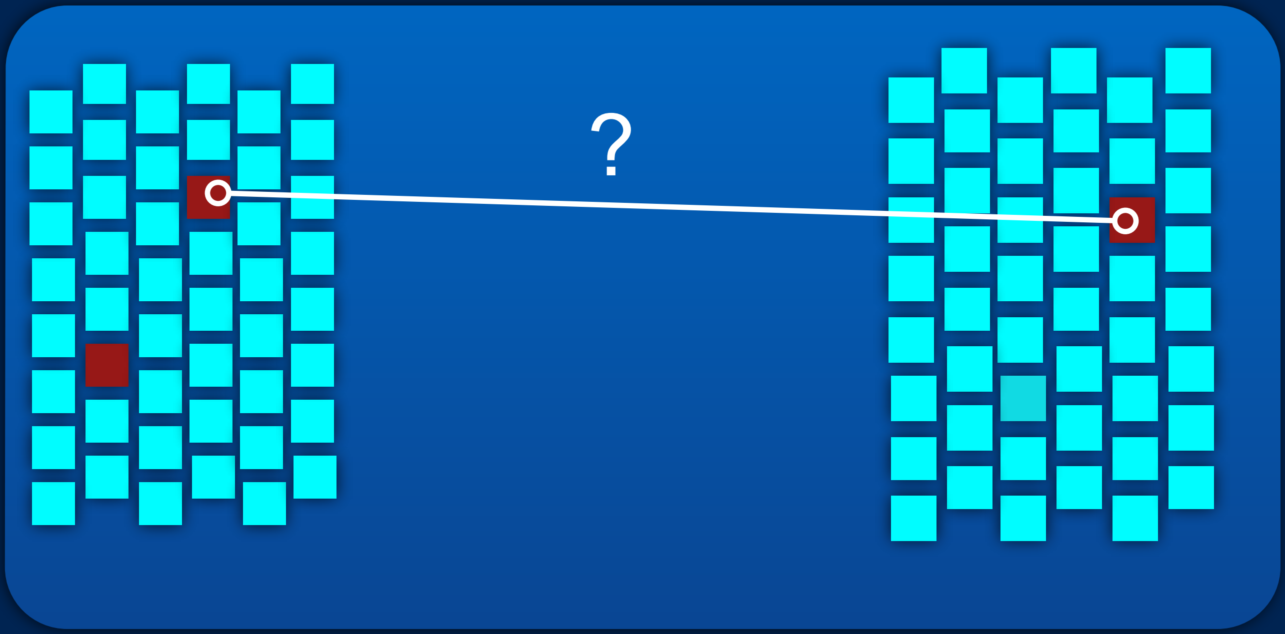
AX-PET yields a large fraction of Inter-Crystal Scatter (ICS) triple events:

→ Enhance sensitivity preserving spatial resolution



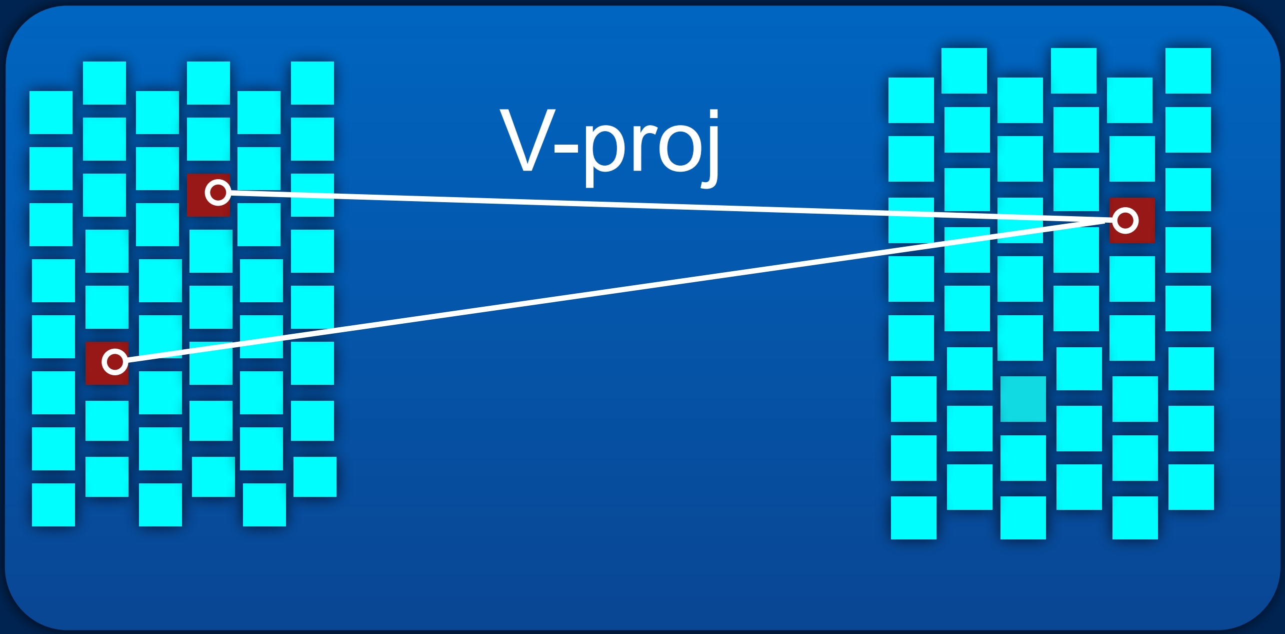


Sensitivity enhance through Triple inclusion



Conventional approach → Identification

- Pre-processing of Triple events to identify the correct LOR
- Computational consuming
- Low identification success rate



Our approach → V-projection

- No identification prior to reconstruction
- V-projection is the new "LOR"
- Full information associated to the Triple event is preserved.

Sensitivity enhance through Triple inclusion

System matrix element

Probability that an annihilation event in voxel j is detected in measurement i

$$n_j^{k+1} = \frac{n_j^k}{\sum_{i=0}^{I} a_{ij}} \sum_{i \in M} \frac{a_{ij}}{\sum_{j=0}^{J} a_{ij} n_j^k}$$

Sensitivity or normalization s_j

Probability that an annihilation event in voxel j is detected

Image at iteration k

And what if a_{ij} is a Triple $a_{i'j}$?

Conventional approach → Identification

$$\frac{a_{i'j}}{\sum_{j=0}^{J} a_{i'j} n_j^k} = \frac{a_{i_t j}}{\sum_{j=0}^{J} a_{i_t j} n_j^k}$$

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

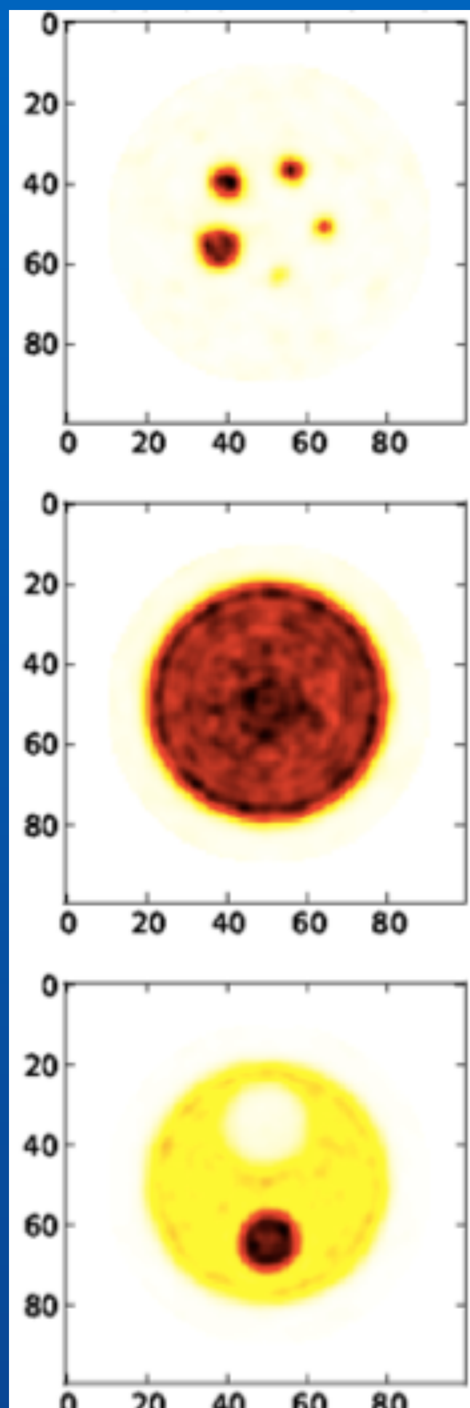
Our approach → V-projection

$$a_{i'j} = \eta_1 a_{i_1 j} + \eta_2 a_{i_2 j}$$

- Both LORs are kept but weights are assigned.
- In **this study, η_t = 0.5** equivalent to randomized selection.

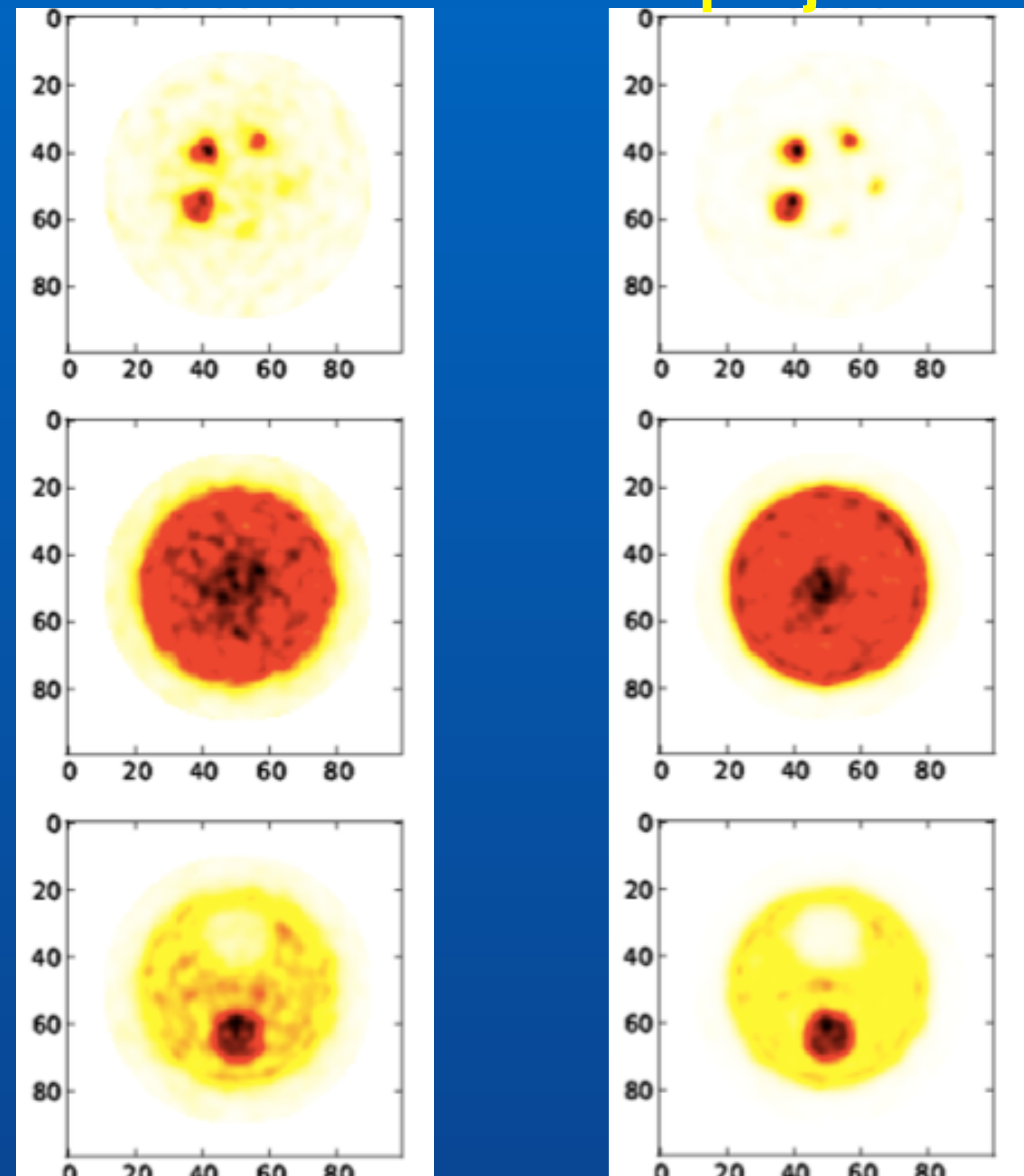
Sensitivity enhance through Triple inclusion

Golden events

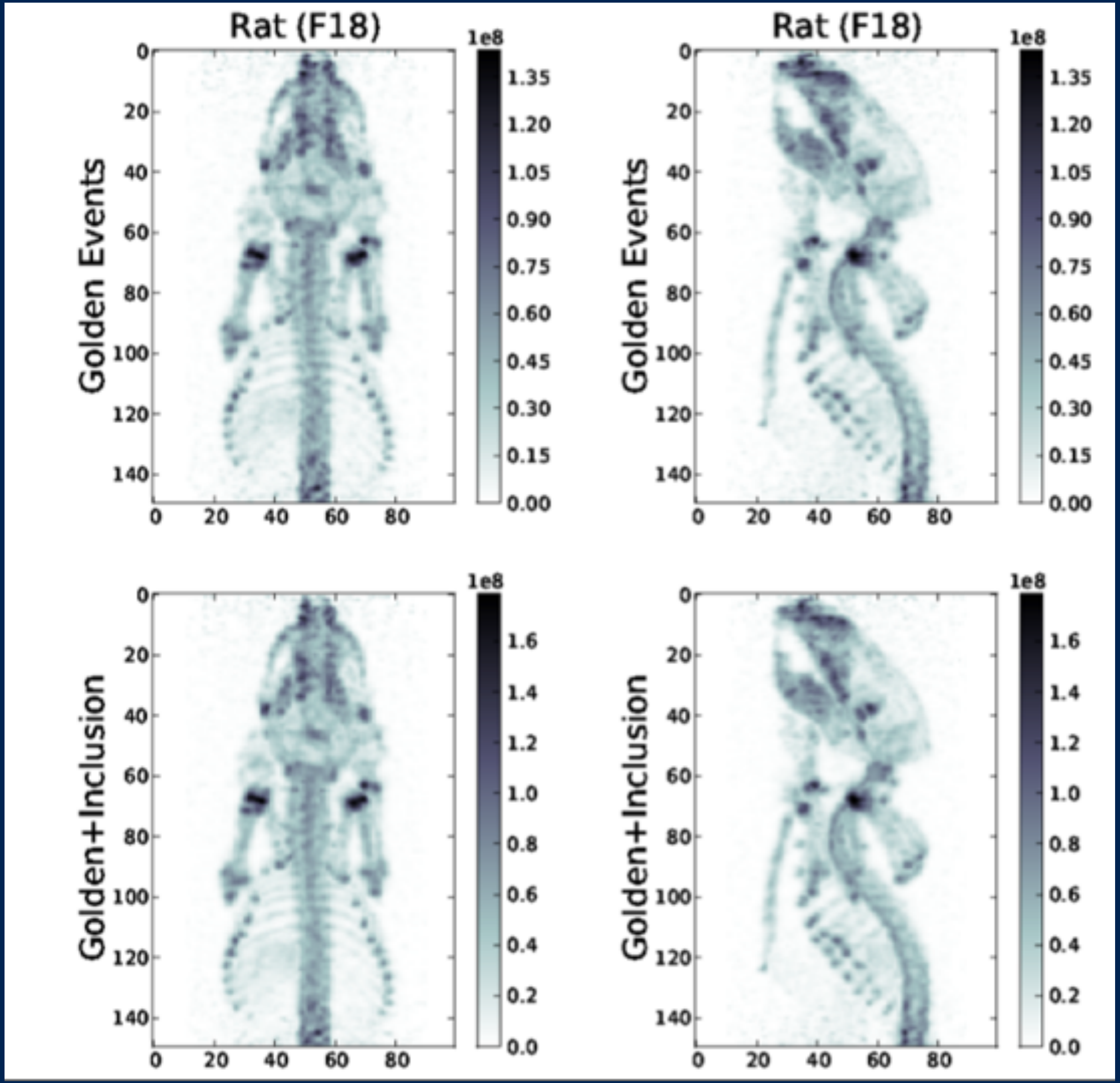


Triple events

Selection | V-projection



Sensitivity enhance through Triple inclusion



- 20% sensitivity increase
- Small increase in SNR (just 10%)
- Difficult to see it by naked eye.
- Spatial resolution preserved.
- Potential in quantification.

Modeling of AX-PET: towards a full scanner

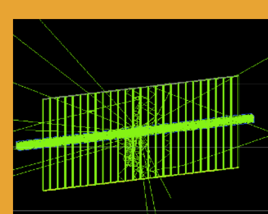
Challenges

- Axially oriented and staggered crystal arrangement → no-conventional geometry
- WLS for axial coordinate → new sensitive elements to be modeled
- Custom made demonstrator electronics → processing of the coincidences

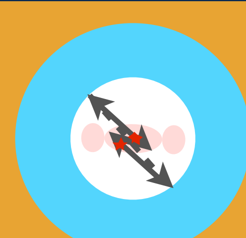
Why Gate? Assessed tool for medical imaging, easy acquisition and source modeling.

GATE modified

Geometrical system description

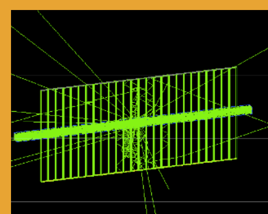


Detector response modeling: WLS+LYSO



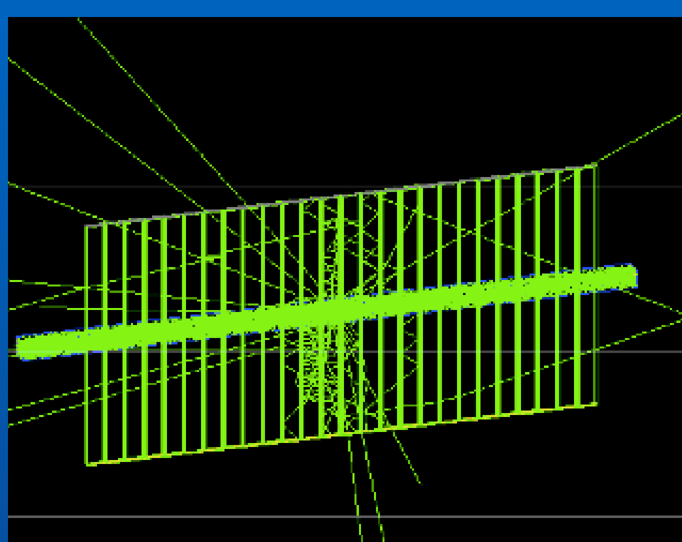
Coincidences and electronics are modeled off-simulation by a dedicated sorter.

Modeling of AX-PET: WLS



Detector response modeling: WLS+LYSO

- Optical simulation is computationally expensive → semi-analytical modeling of WLS response is chosen.
- Pure resolution model is not enough → electronics dead-time depends on WLS channels too.

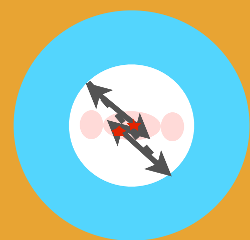


- Optical simulation by Geant4 of the full WLS hodoscope and LYSO.
- Analytical model parameters tuned.

$$N_{pe(i)} = \sum_{n=1}^{N} A(x_n, E_n) \cdot e^{\frac{(z_n - z_i)^2}{2\sigma_{x_n}^2}}$$

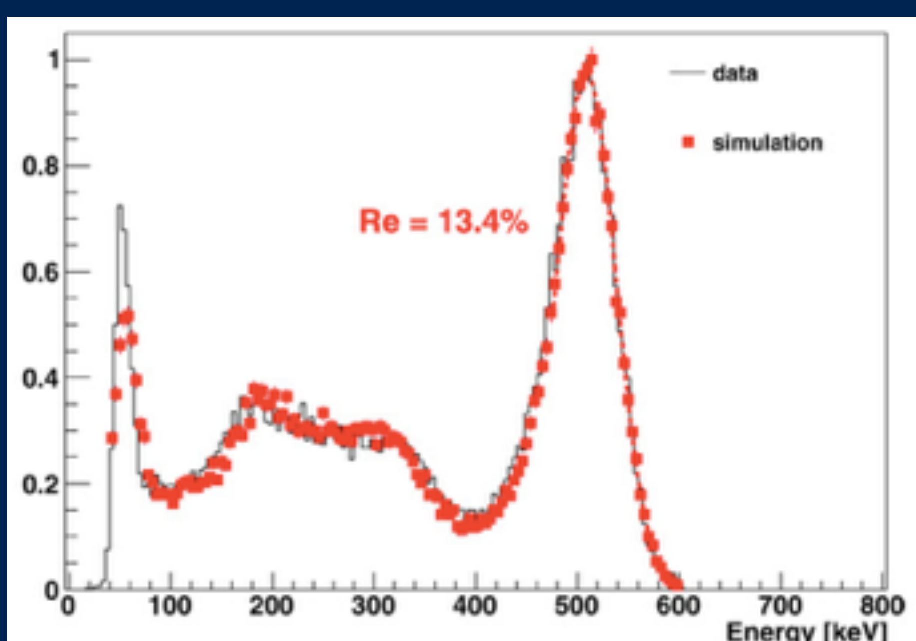
For each Single, the signal distribution on the WLS hodoscope is computed and stored in the root output.

Modeling of AX-PET: coincidence sorting



Coincidences and electronics are modeled off-simulation by a dedicated sorter.

- Electronics non-optimized for PET acquisitions → off-line processing of the coincidences.
- New sensitive elements as WLS → new digitizer unit for thresholding signal.

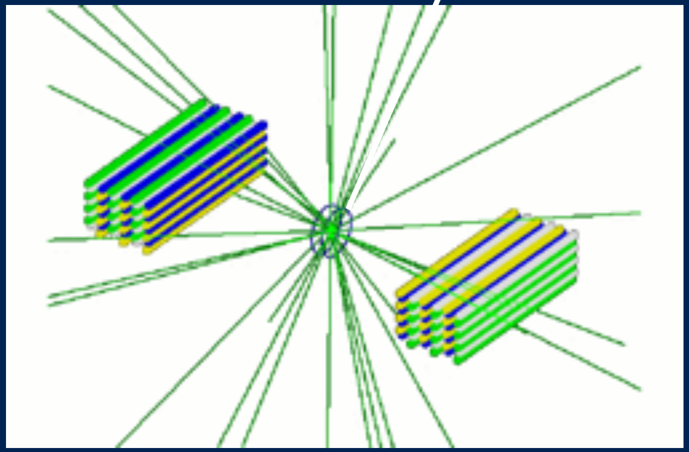


Read-out logic

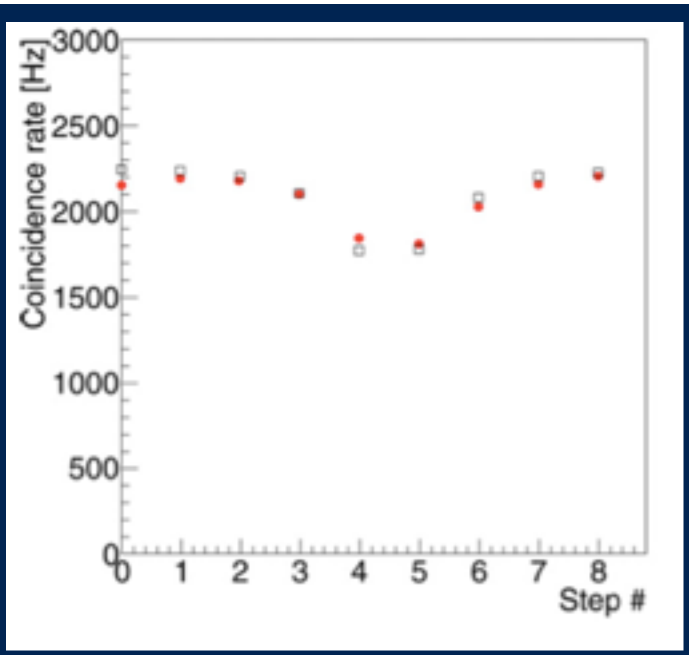
- Threshold at Single Level (LL~50 keV)
- Pile-up at module level (t_{pu}~250 ns)
- Threshold at module level HL~400 keV and HHL~600 keV
- Coincidence between two modules τ_w = 20 ns
- Dead-time parameterized τ_{dt}

Modeling of AX-PET: coincidence sorting

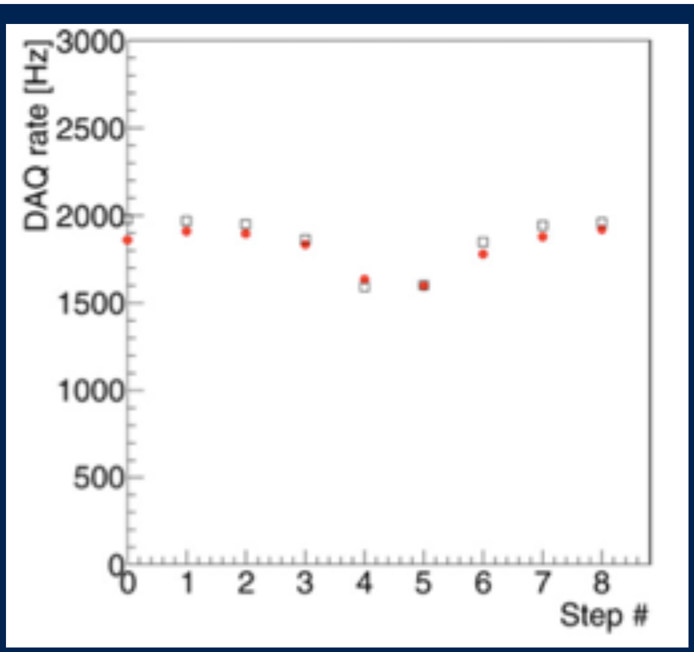
^{22}Na source



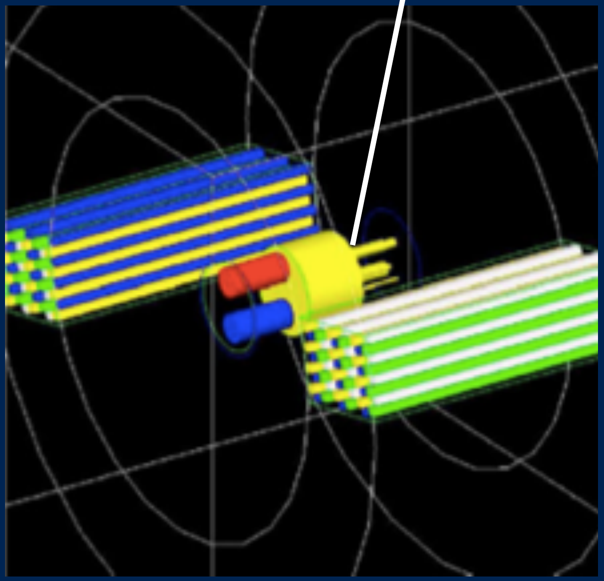
Pre-deadtime

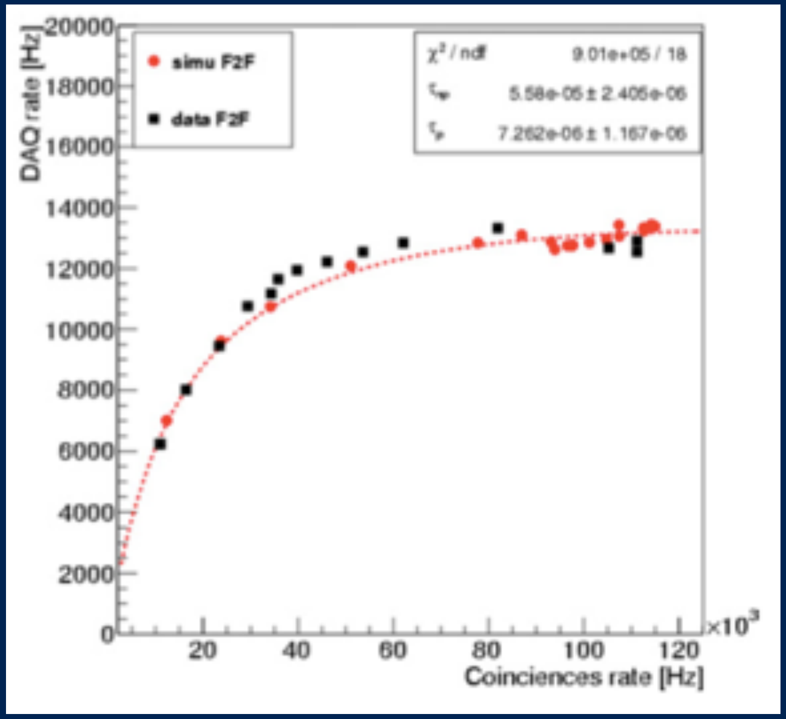


Post-deadtime



NEMA phantom

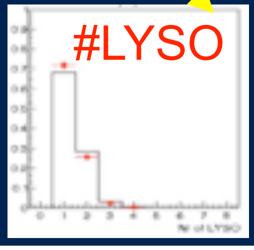


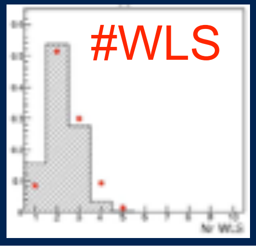


Hybrid paralizable into non-paralizable dead-time model

$$R_{\mathrm{DAQ}} = \frac{R_t \cdot e^{-R_t \tau_p}}{1 + \tau_{np} \cdot R_t \cdot e^{-R_t \tau_p}}$$

$$\tau_{\mathrm{dt}} = N_{\mathrm{wc}} \times \tau_{\mathrm{wc}} + \tau_0 (\mu s)$$

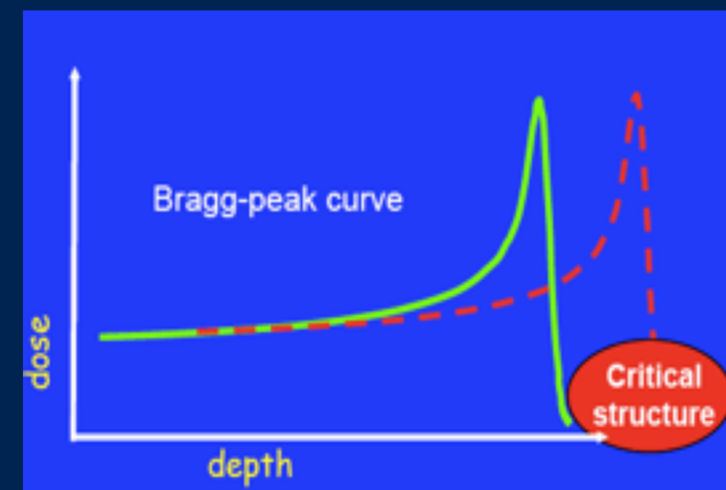


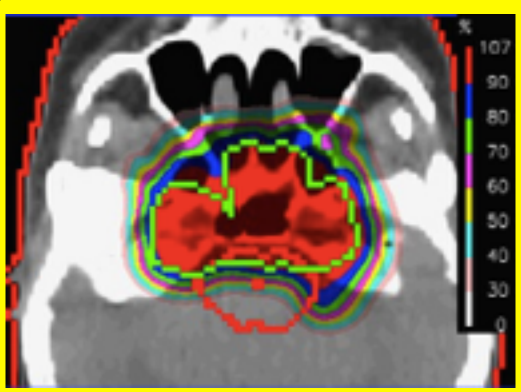


Hadron-therapy monitoring

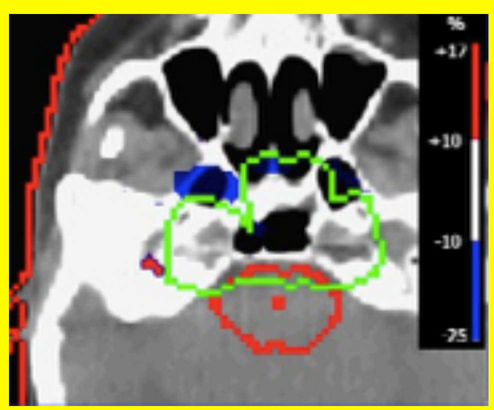
Advantage of hadrons is that they fully stop within the patient, with high dose release at the end.

…but we don't know exactly where.

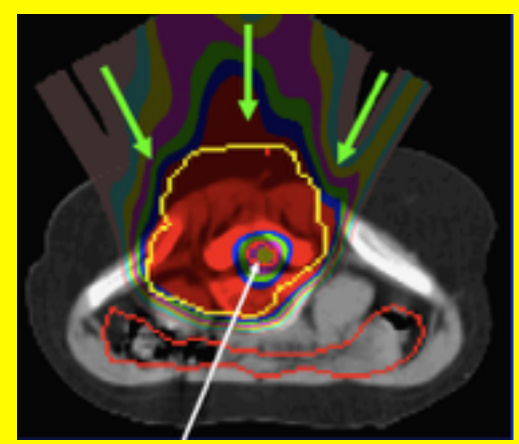




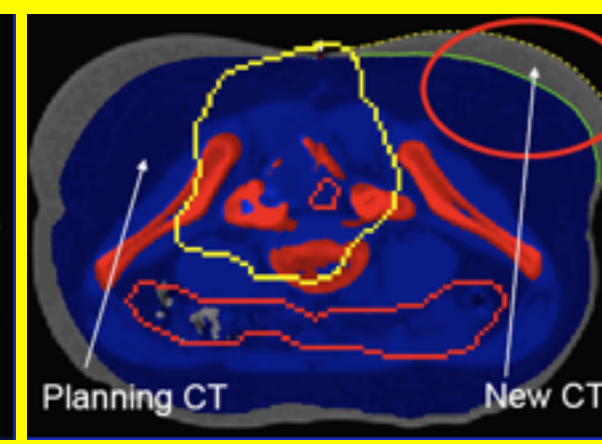
Normal p plan 3 ports



Differences after CT correction



Sparing spinal cord at centre of PTV

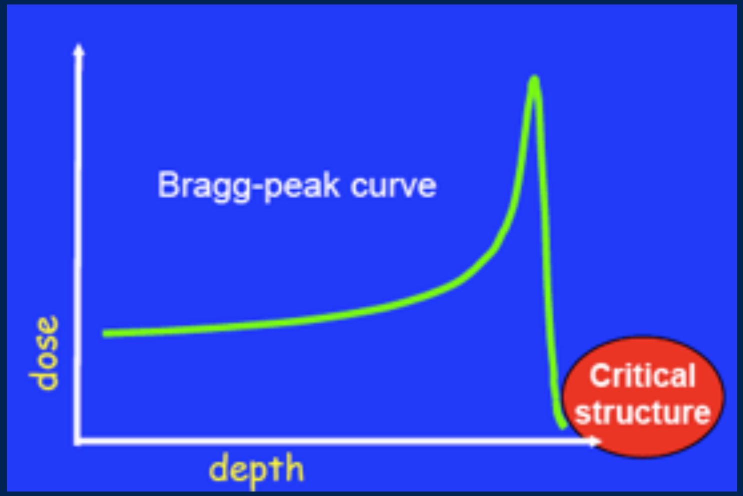


1.5 kg gain weight

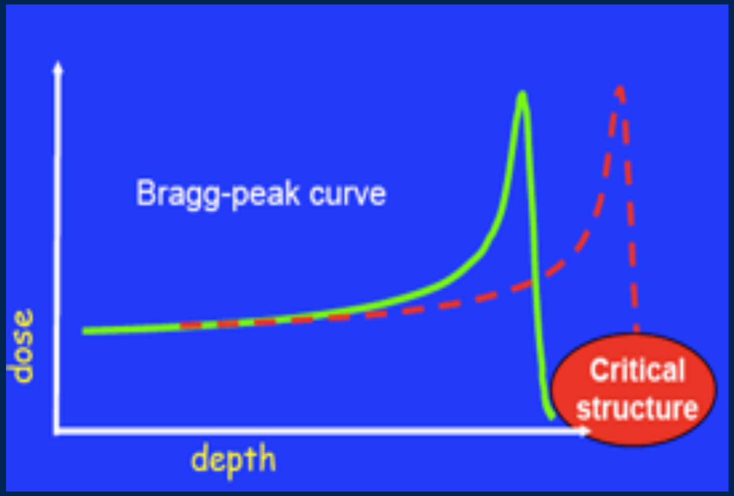
***courtesy of T. Lomax**

Hadron-therapy monitoring

Advantage of hadrons is that they fully stop within the patient, with high dose release at the end.

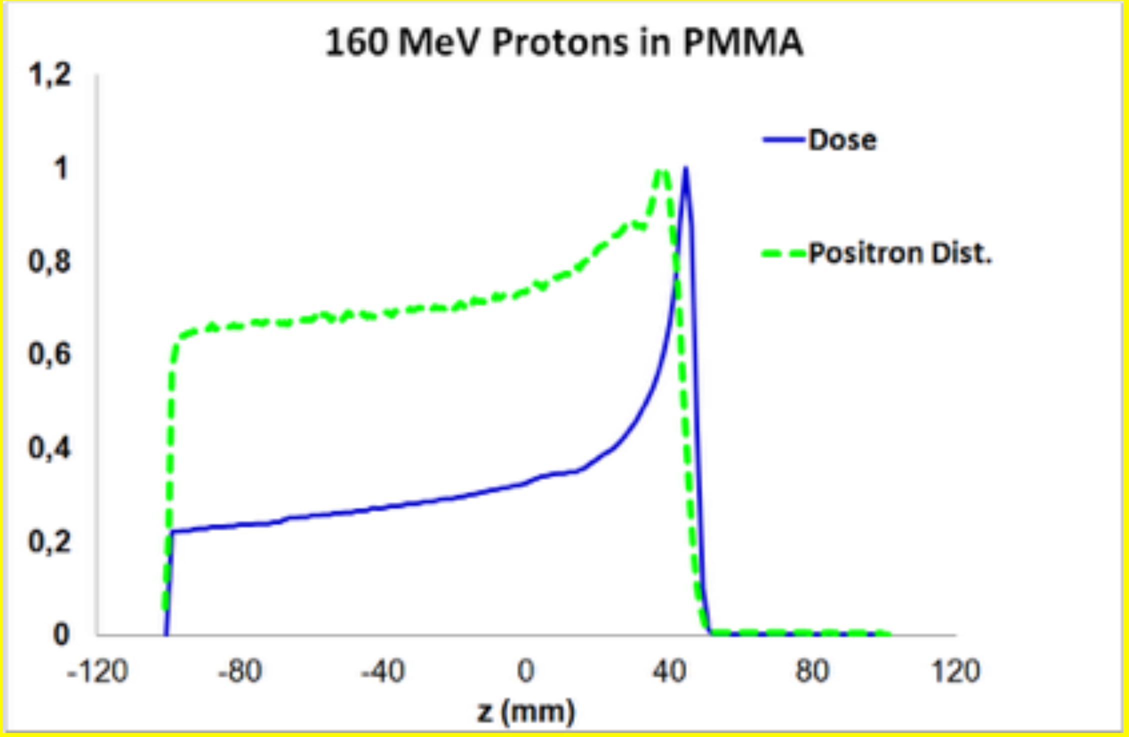


…but we don't know exactly where.



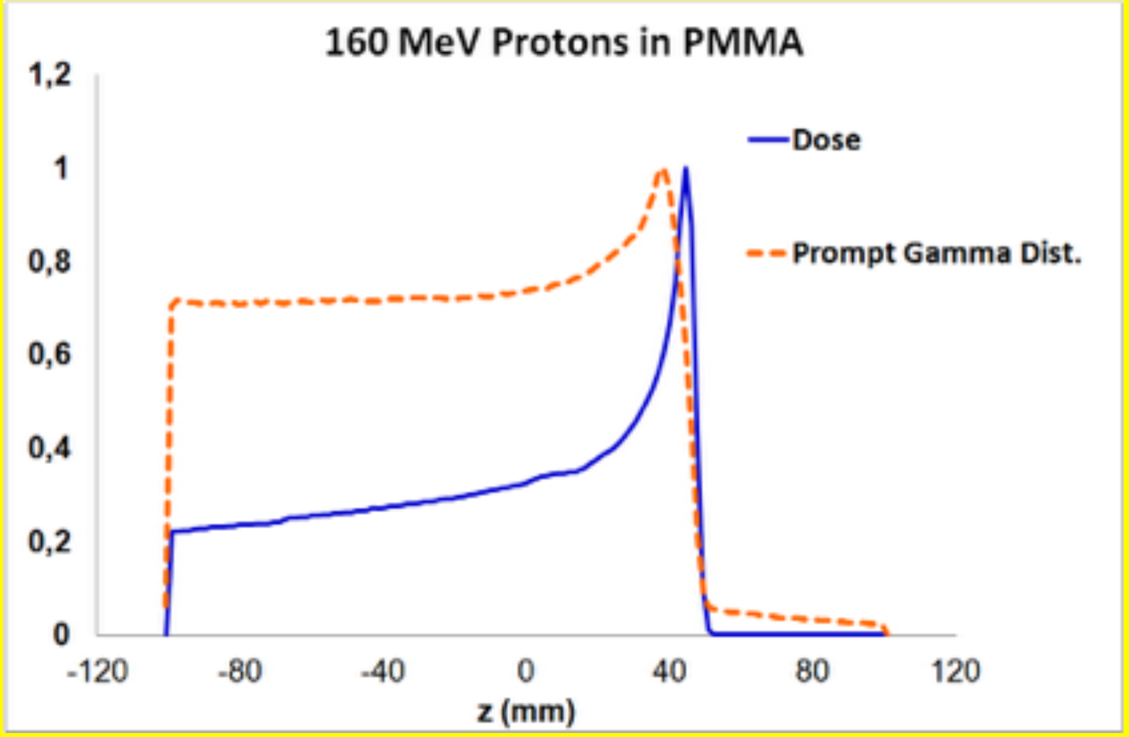
How can we know we did everything correctly?

Hadron-therapy monitoring



Positron emitters (^{11}C, ^{10}C, ^{15}O, ^{13}N)

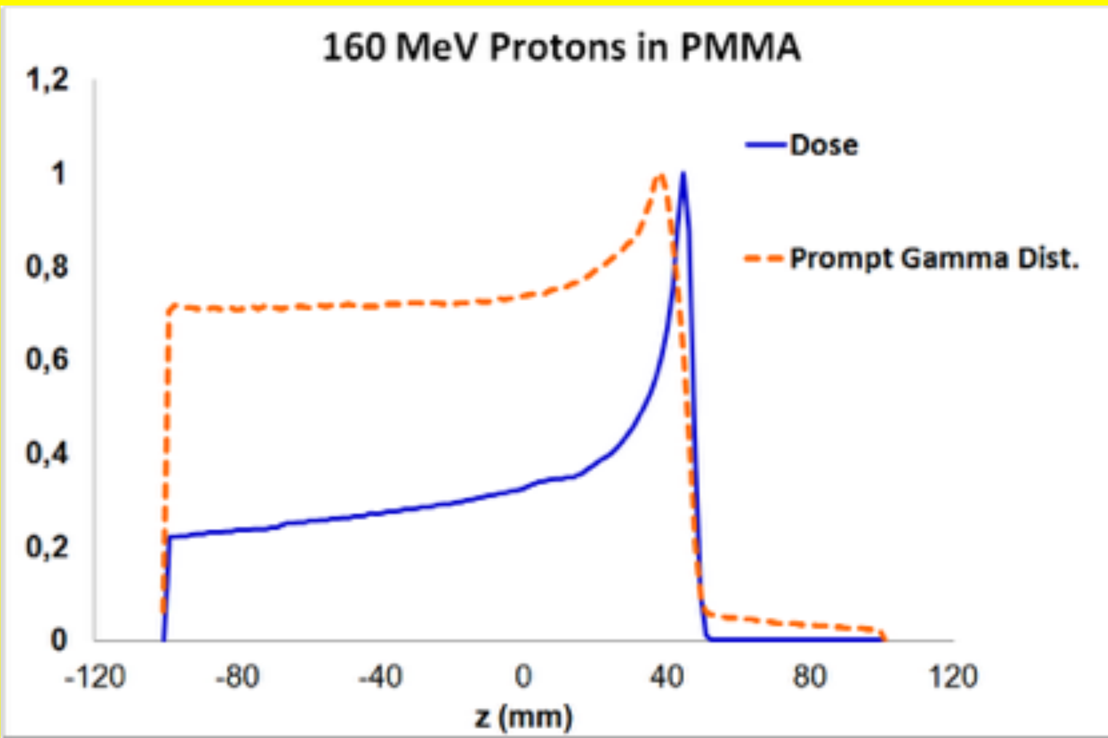
- PET imaging
- assessed technique
- low sensitivity



Prompt gammas (1-15 MeV)

- Compton Imaging
- novel technique
- noise? sensitivity? resolution?

Hadron-therapy monitoring



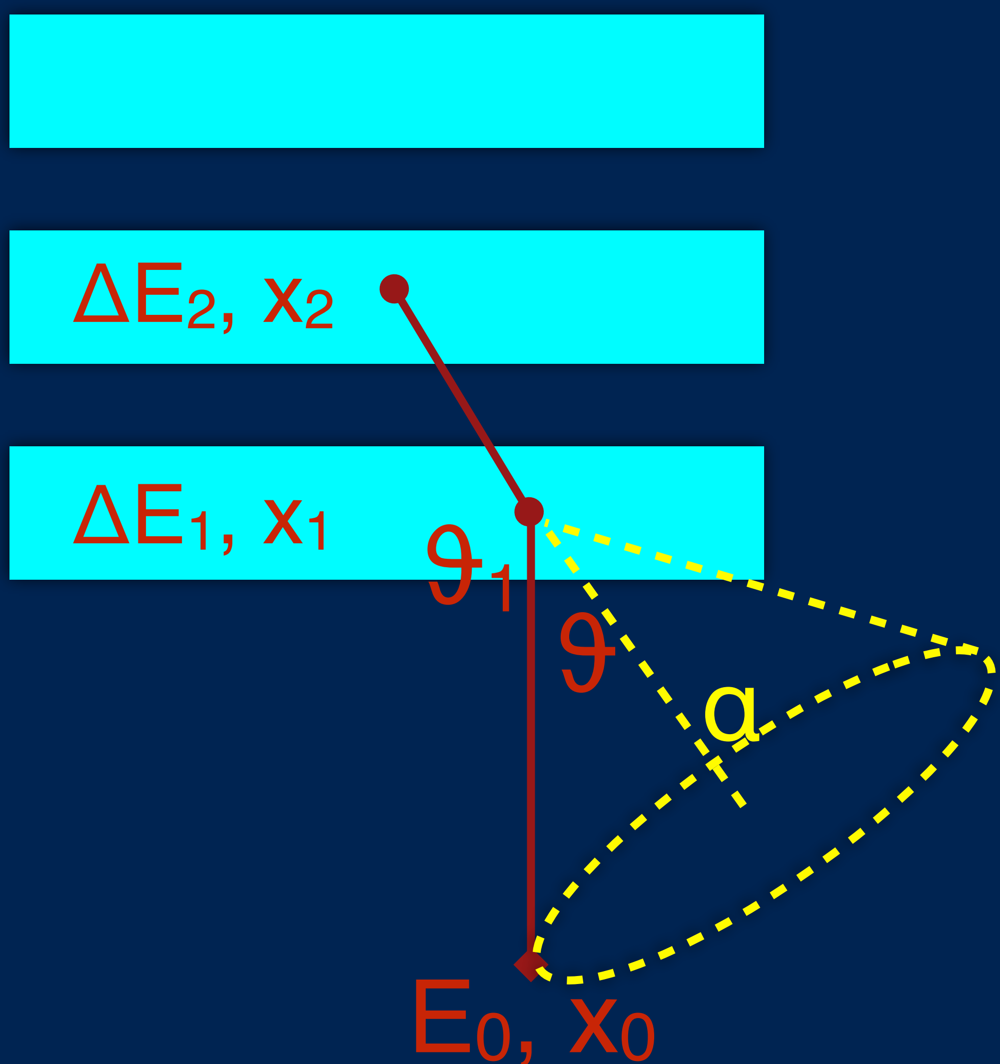
Prompt gammas (1-15 MeV)

- Compton Imaging
- novel technique
- noise? sensitivity? resolution?

MACACO
Medical Application
CompAct Compton camera

Three layer Compton Telescope based on monolithic LaBr crystals.

Compton Telescope image reconstruction



Main features

- The incoming γ track must be on the cone surface.
- x_1 and x_2 provide the cone axis α and the energy the cone aperture ϑ

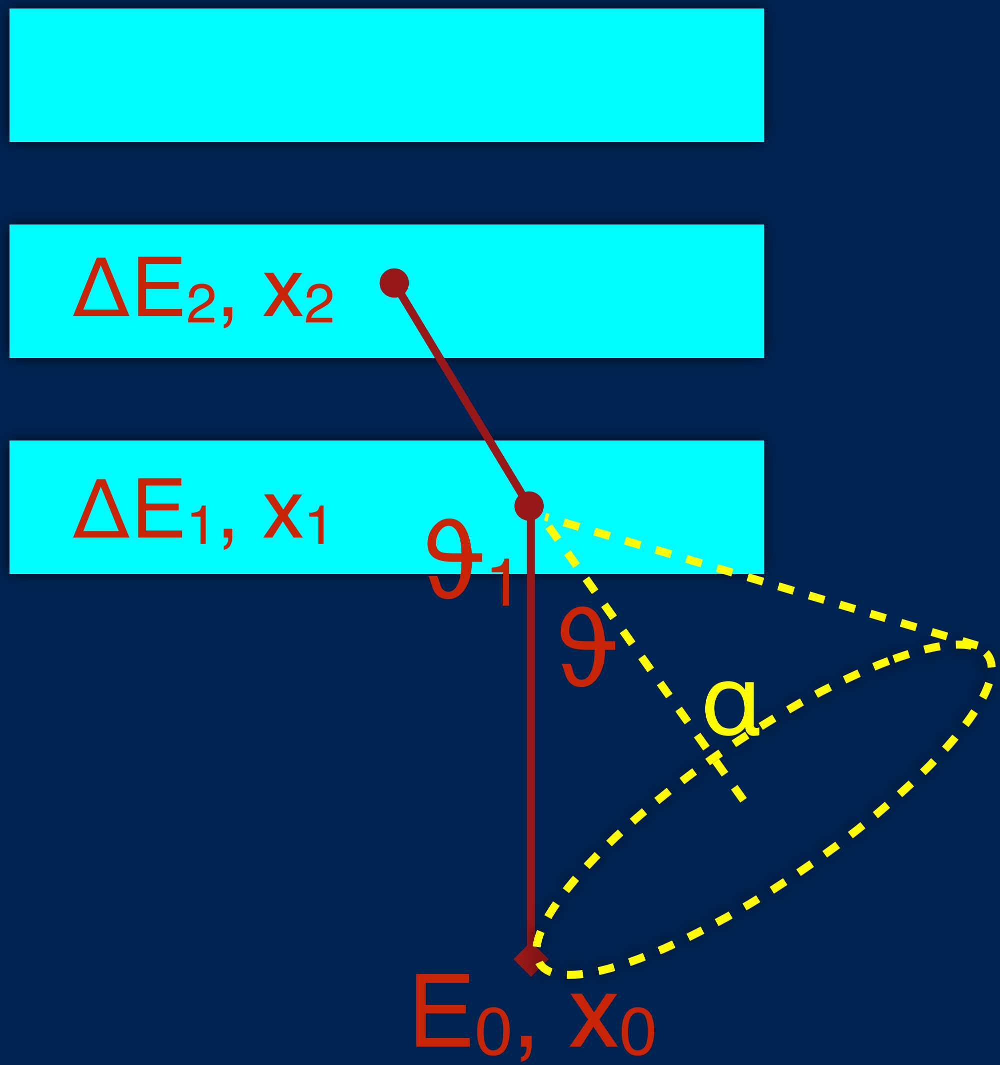
$$\cos\vartheta = 1 + m_0c^2(E_0^{-1} + (E_0-\Delta E_1)^{-1})$$

The energy $\mathbf{E_0}$ can be:

Estimated, if we assume evt. 2 is a photoelectric

$$E_0 = \Delta E_1 + \Delta E_2$$

Compton Telescope image reconstruction



The energy $\mathbf{E_0}$ can be:

Estimated, if we assume evt. 2 is a photoelectric

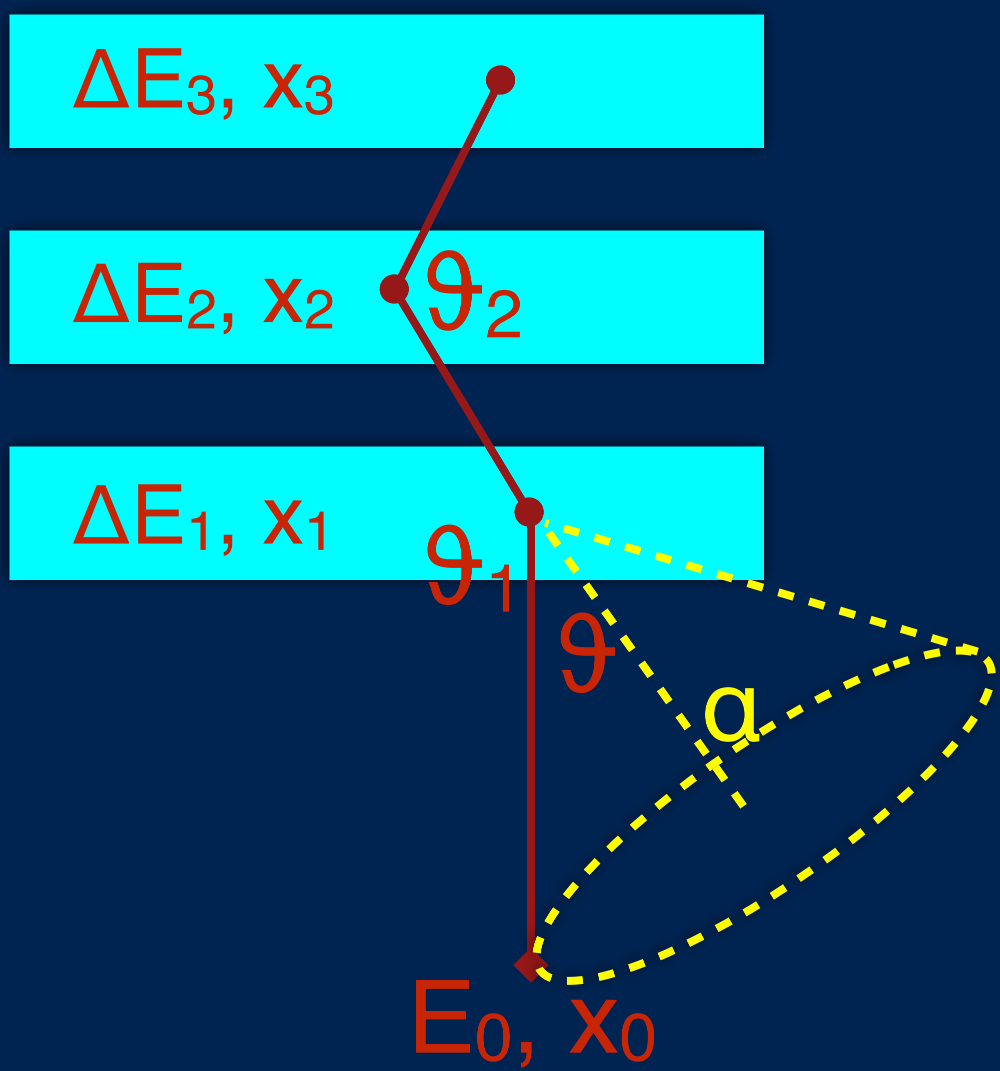
$$E_0 = \Delta E_1 + \Delta E_2$$

Most probably this condition doesn't hold!!

Assumed, if we consider a wider energy energy of the incoming photon and perform a spectral reconstruction

E_0 in $[\Delta E_1 + \Delta E_2$, max energy$]$

Compton Telescope image reconstruction



The energy $\mathbf{E_0}$ can be **measured**

- x_1 and x_2 provide the cone axis α and the energy the cone aperture ϑ
- Knowing of two photons vectors and three energies provides the initial gamma energy:

$$\mathbf{E_0} = \Delta E_1 + 0.5\left(\Delta E_2 + \left(\Delta E_2^2 + \frac{4\Delta E_2 m_0 c^2}{1-\cos\vartheta_2}\right)^{0.5}\right)$$

- More complexity of the data: ordering, random contamination.
- Less sensitivity.

Compton Telescope image reconstruction

- **MLEM** based reconstruction algorithms.
- **Sensitivity** to measurements over the FOV is assumed constant
- **Post-reconstruction** image co-registration of different reconstructed images not faced yet

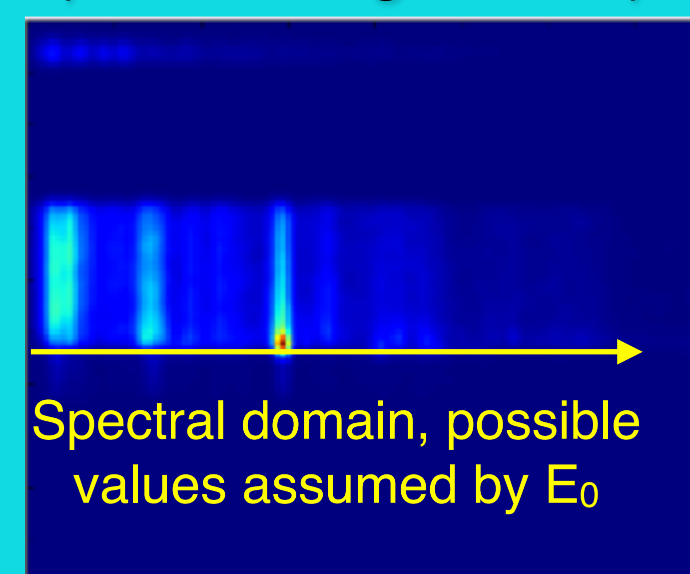
E_0 measured - 3I

- **Resolution model** to be applied to the image space and expressed as angular blurring
- System response calculated from **minimum distance between voxel and cone surface**

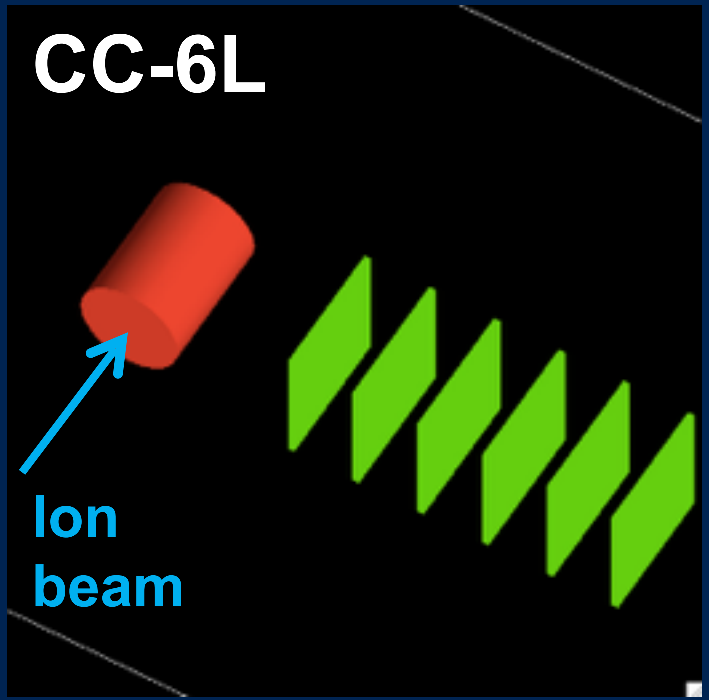
E_0 assumed - 2I

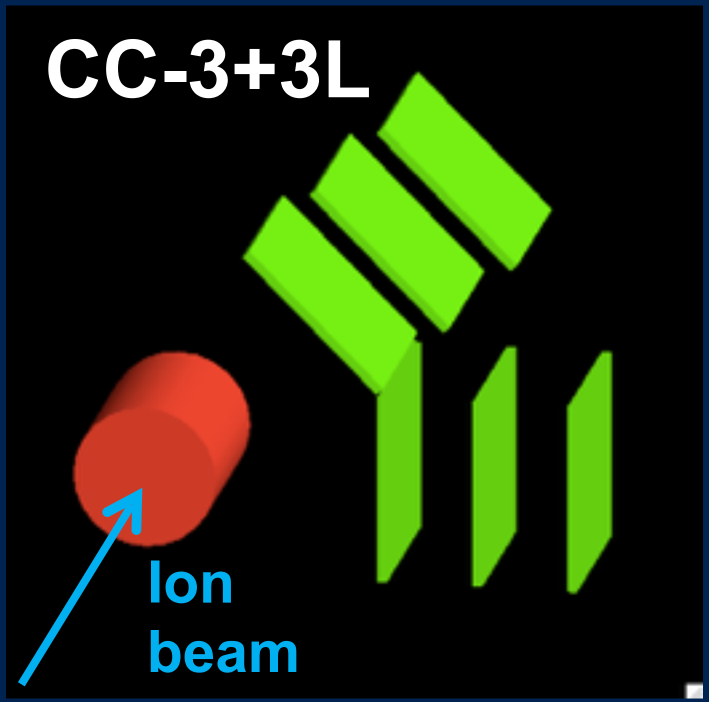
As in E0 measured but…

- Image space extended to a **4th dimension** over a given energy range.
- **GPU** extension, pyCUDA, employed.
- Post-reconstruction processing of the spectral images is required.



Enhanced sensitivity configuration



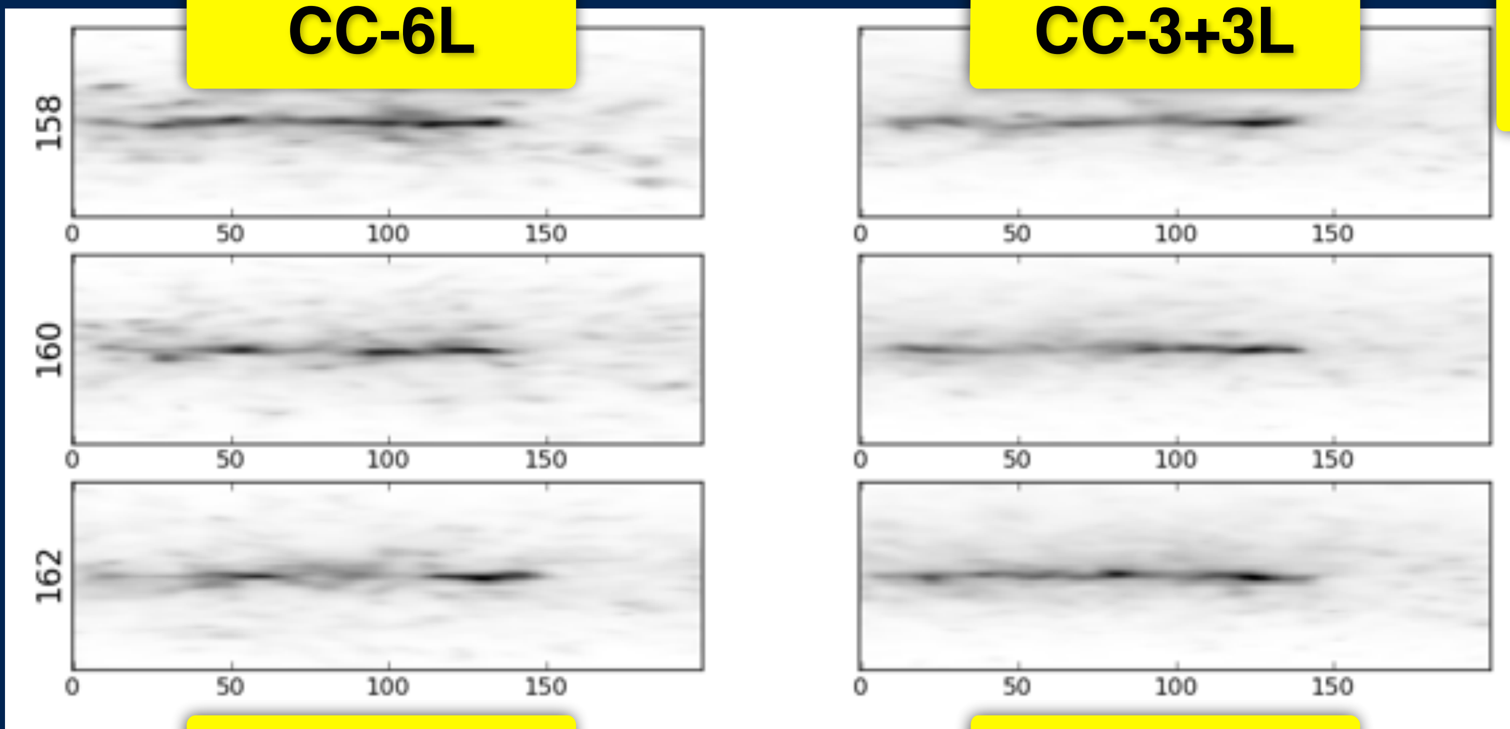


- Proton beam 160 MeV, $5x10^7$ flux entering a cylindrical PMMA phantom.
- Geant4.9.3
  - 1Co+1Co/Pho (2l)
  - 1Co+1Co+1Co/Pho (3l)

Two configurations have been studied having an increased sensitivity: a 6 layer Compton Telescope and 2 Compton Telescopes of 3 layers each, both perpendicularly placed to the beam entering the phantom.

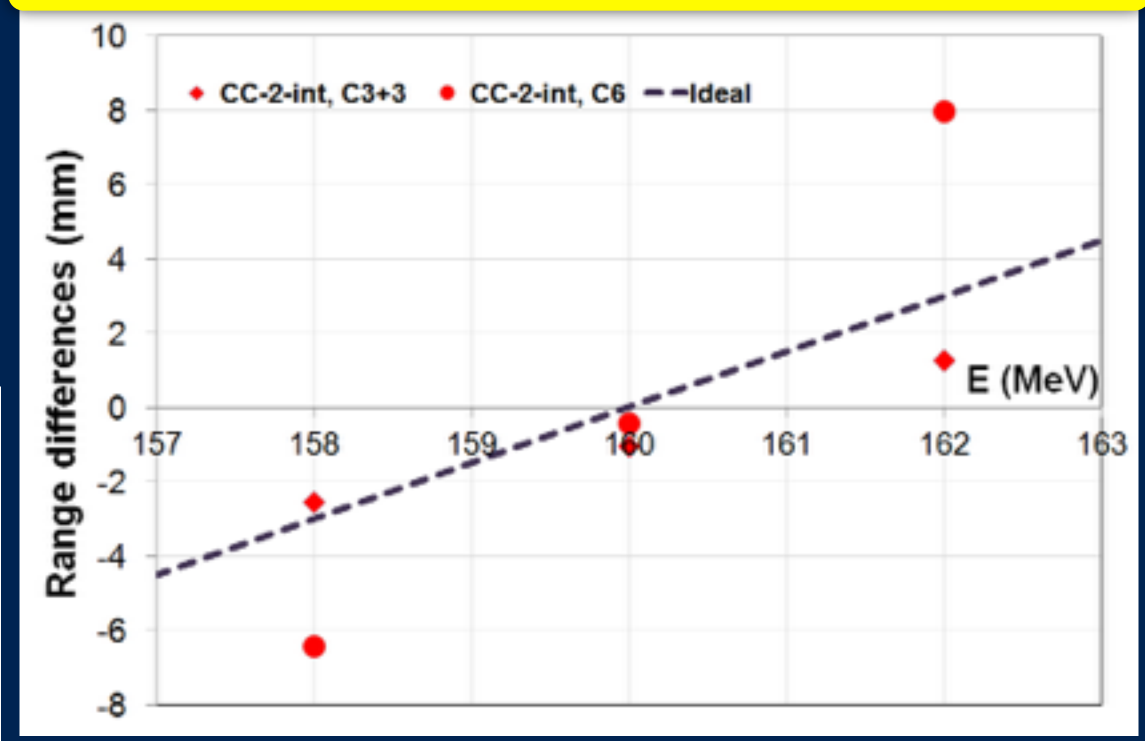
Enhanced sensitivity configuration

CC-6L **CC-3+3L**

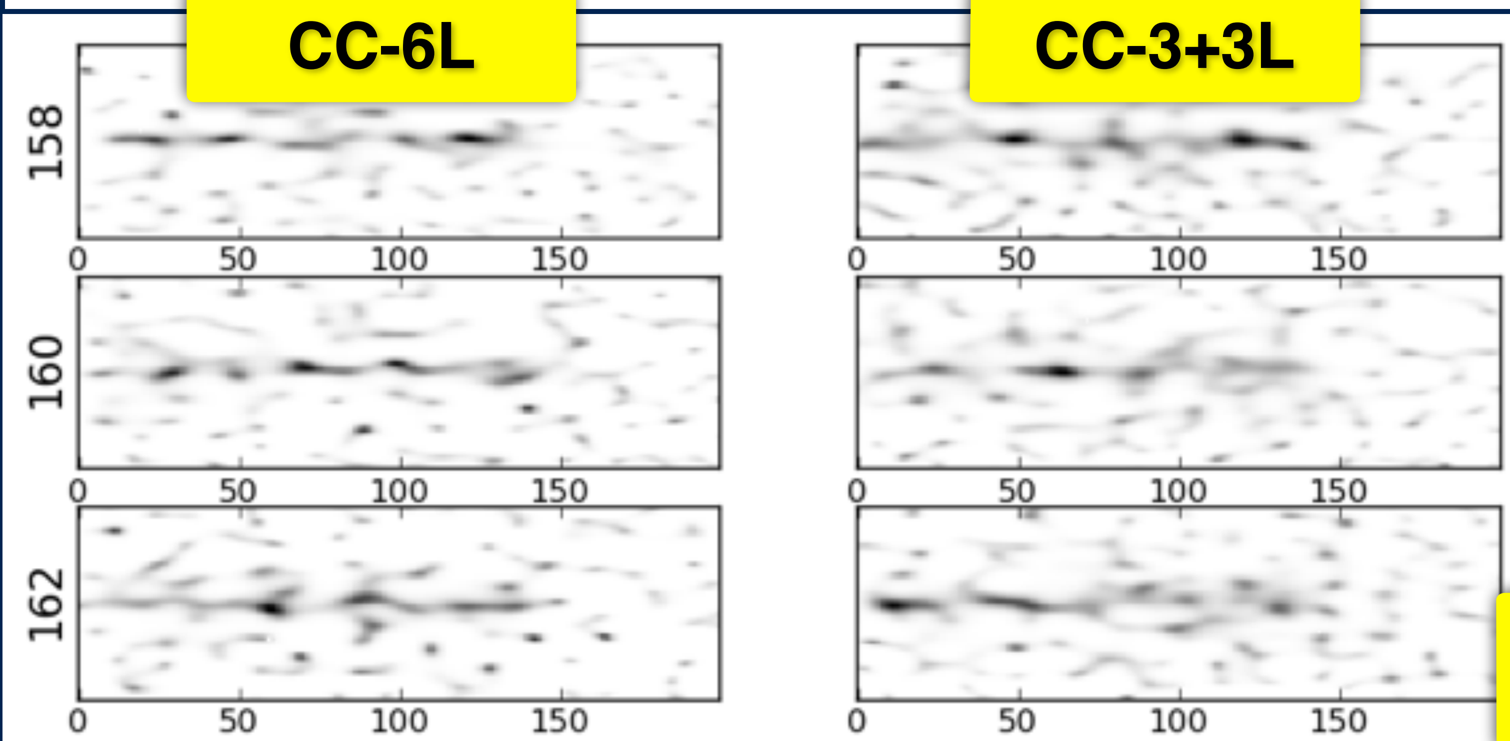


2l spectral reconstruction
30-th interaction, voxel 5x1mm^2

Range calculation from prompt gammas for different p energies (R50)



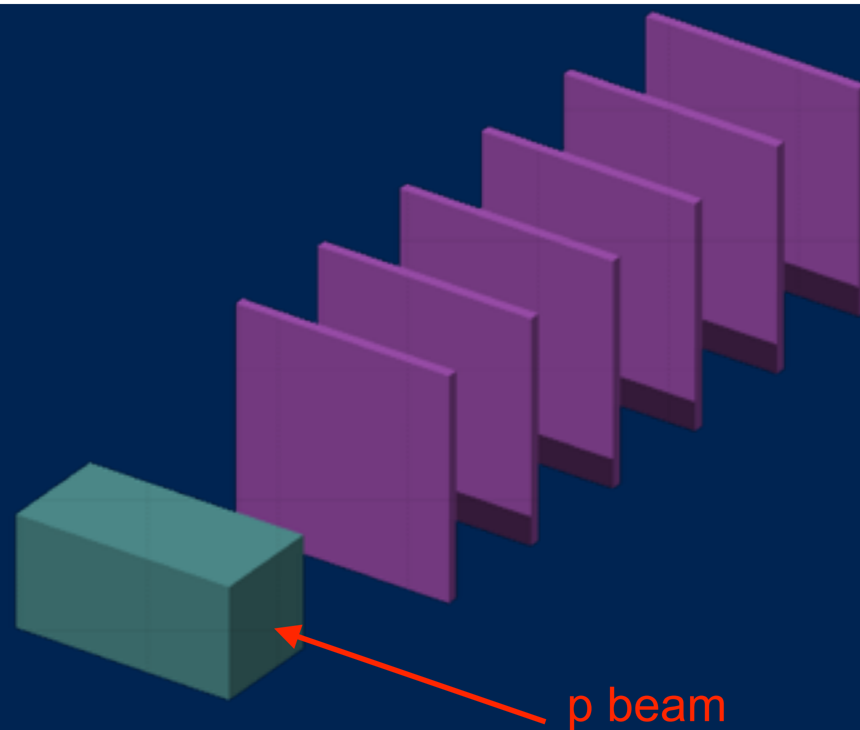
CC-6L **CC-3+3L**



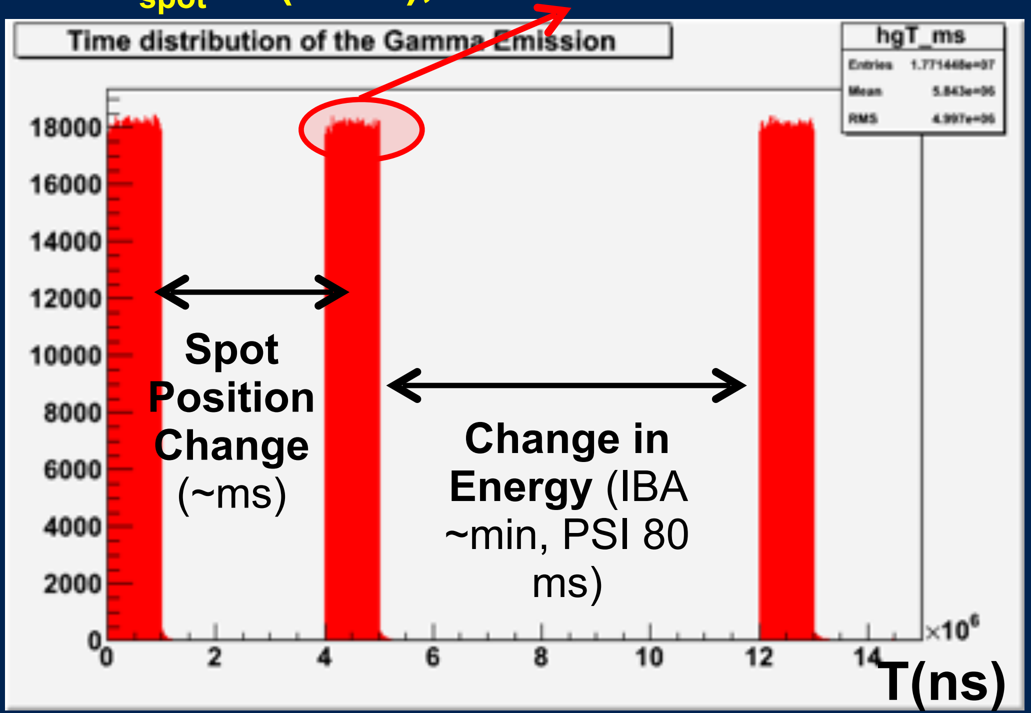
3l
30-th interaction, voxel 5x1mm^2

Effect of neutrons and random events

- FLUKA is employed and the time structure of the beam is included.
  - E = 100, 140, 180 MeV p
  - Total fluence 5×10^8
- Reference beam model: the IBA isochronus cyclotron.



T_{spot} = f(dose), from 1 to 30 ms



Applying time structure to the beam

↓

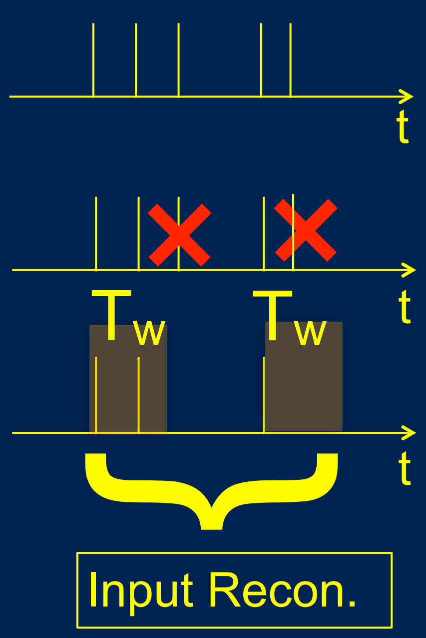
Selection of interactions in the CC

↓

Selection of coincidences in CC with T_w

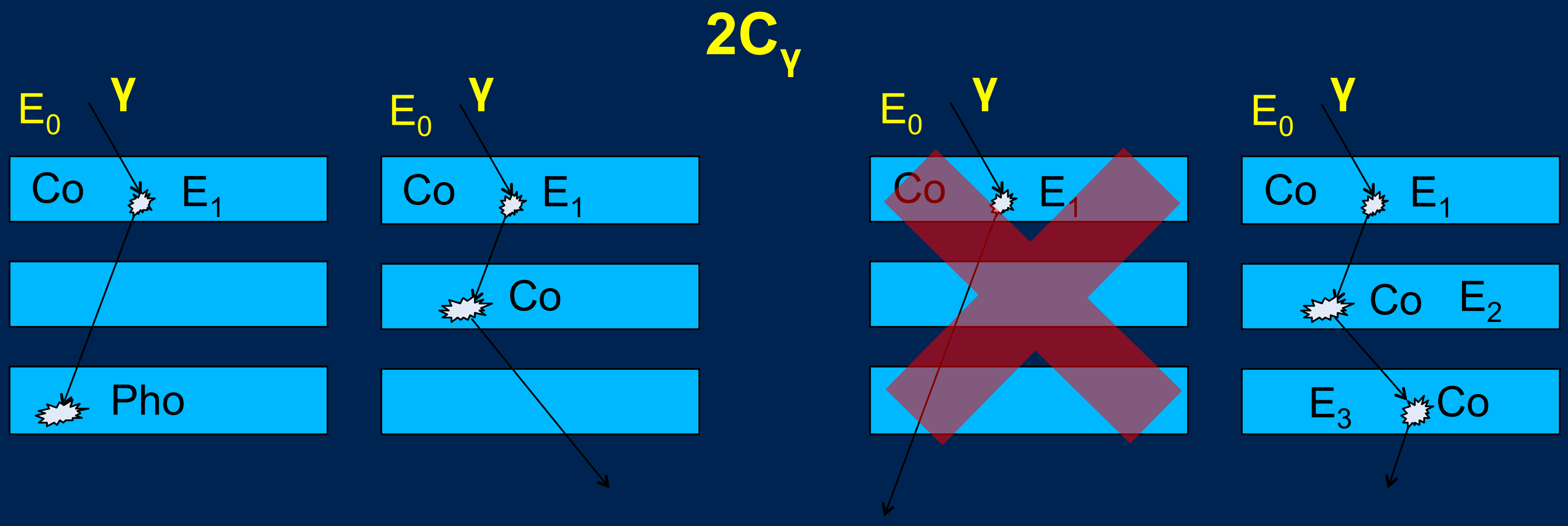
↓

Reconstruction of coincidence



Data preparation (I)

• 2Cγ: Scoring of gamma track interactions with two or more than two interactions, without neutrons
• 1Cγ: Scoring of gamma track interactions with one or more than one interactions, without neutrons
• 2Cγ+n: Scoring of gamma and neutrons tracks interactions with two or more than two interactions
• 1Cγ+n: Scoring of gamma and neutrons tracks interactions with one or more than one interactions



Data preparation (II)

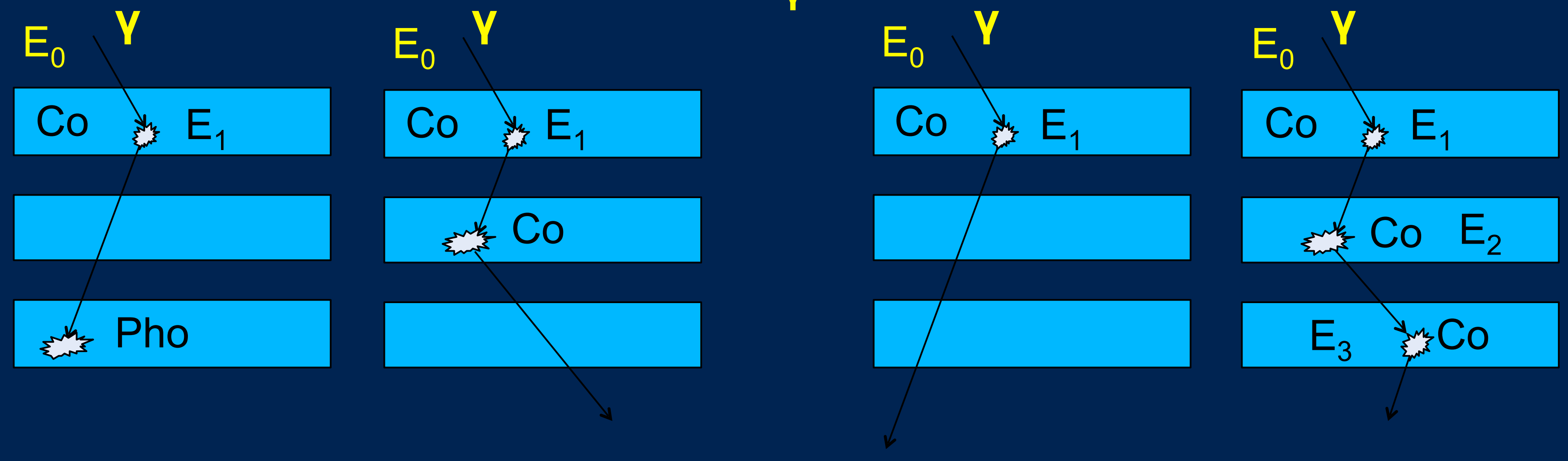
• 2Cγ: Scoring of gamma track interactions with two or more than two interactions, without neutrons

• 1Cγ: Scoring of gamma track interactions with one or more than one interactions, without neutrons

• 2Cγ+n: Scoring of gamma and neutrons tracks interactions with two or more than two interactions

• 1Cγ+n: Scoring of gamma and neutrons tracks interactions with one or more than one interactions

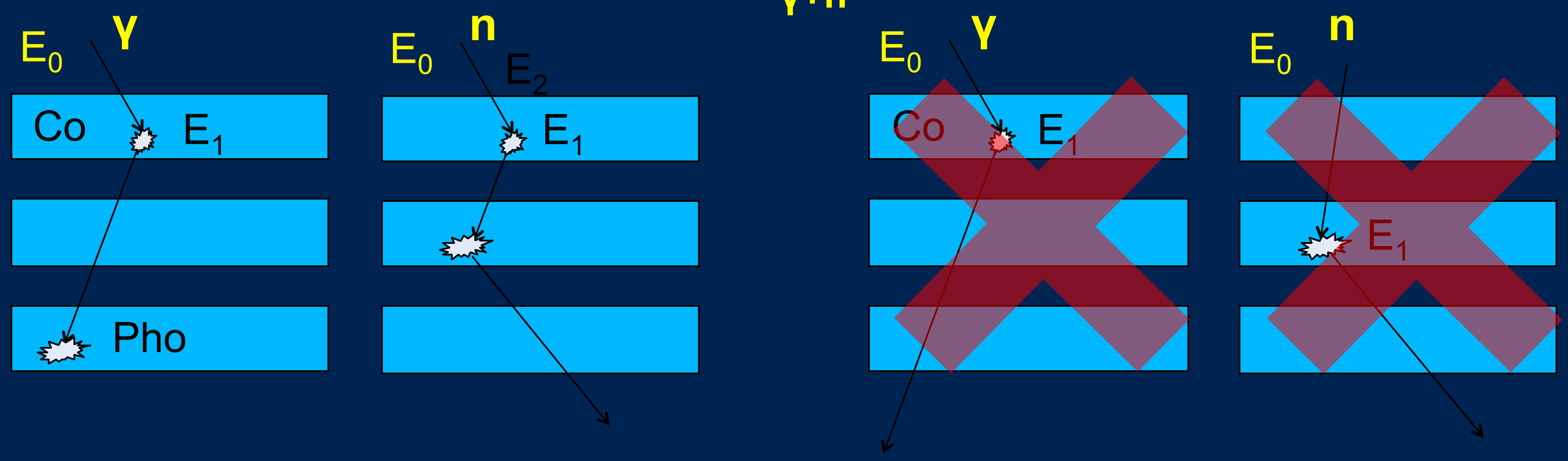
$1C_\gamma$



Data preparation (III)

- $2C_\gamma$: Scoring of gamma track interactions with two or more than two interactions, without neutrons
- $1C_\gamma$: Scoring of gamma track interactions with one or more than one interactions, without neutrons
- $2C_{\gamma+n}$: Scoring of gamma and neutrons tracks interactions with two or more than two interactions
- $1C_{\gamma+n}$: Scoring of gamma and neutrons tracks interactions with one or more than one interactions

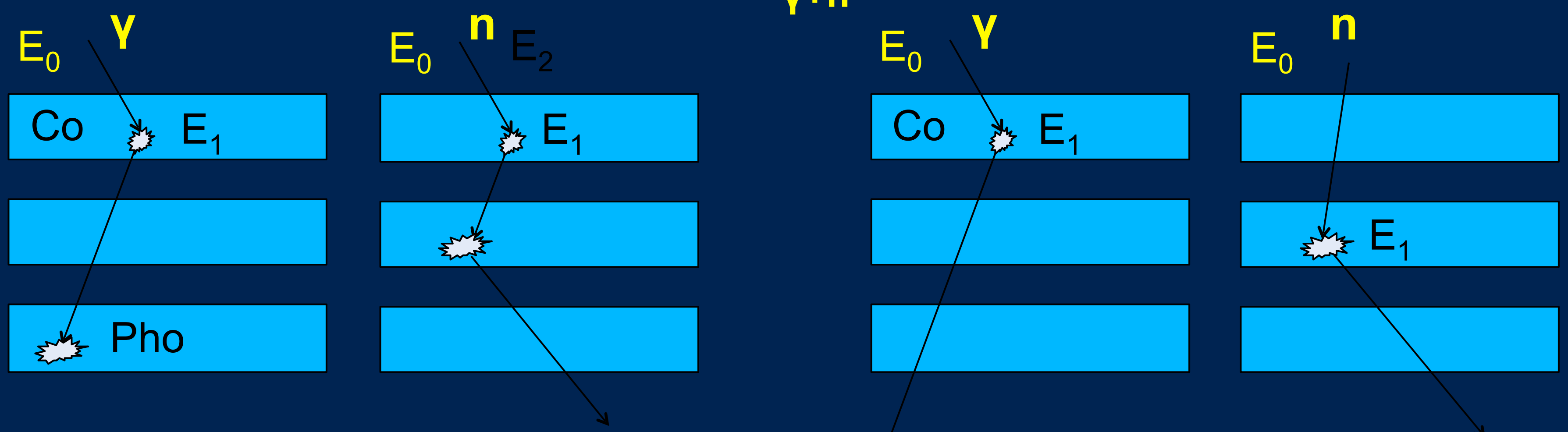
$2C_{\gamma+n}$



Data preparation (IV)

- 2Cγ: Scoring of gamma track interactions with two or more than two interactions, without neutrons
- 1Cγ: Scoring of gamma track interactions with one or more than one interactions, without neutrons
- 2Cγ+n: Scoring of gamma and neutrons tracks interactions with two or more than two interactions
- 1Cγ+n: Scoring of gamma and neutrons tracks interactions with one or more than one interactions

$1C_{\gamma+n}$



- Once interactions have been selected, **time window to select coincidence** events is applied.
- Two time windows are studied: **2 and 0.75 ns**.
- Two kind of random events: two uncorrelated prompt gammas or a prompt gamma with a neutron event.

Reconstructed images with neutrons and random events

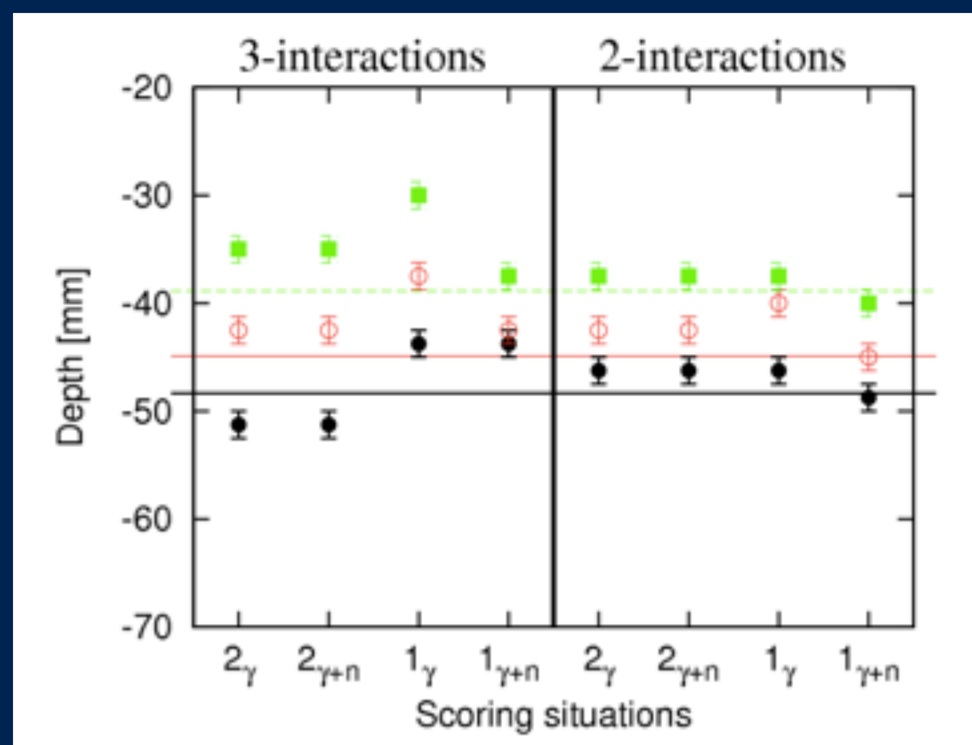
Gamma rate

E(MeV)	$R_\gamma(10^8 p/s)$
100	*0.3387*
140	*1.3387*
180	*3.4681*

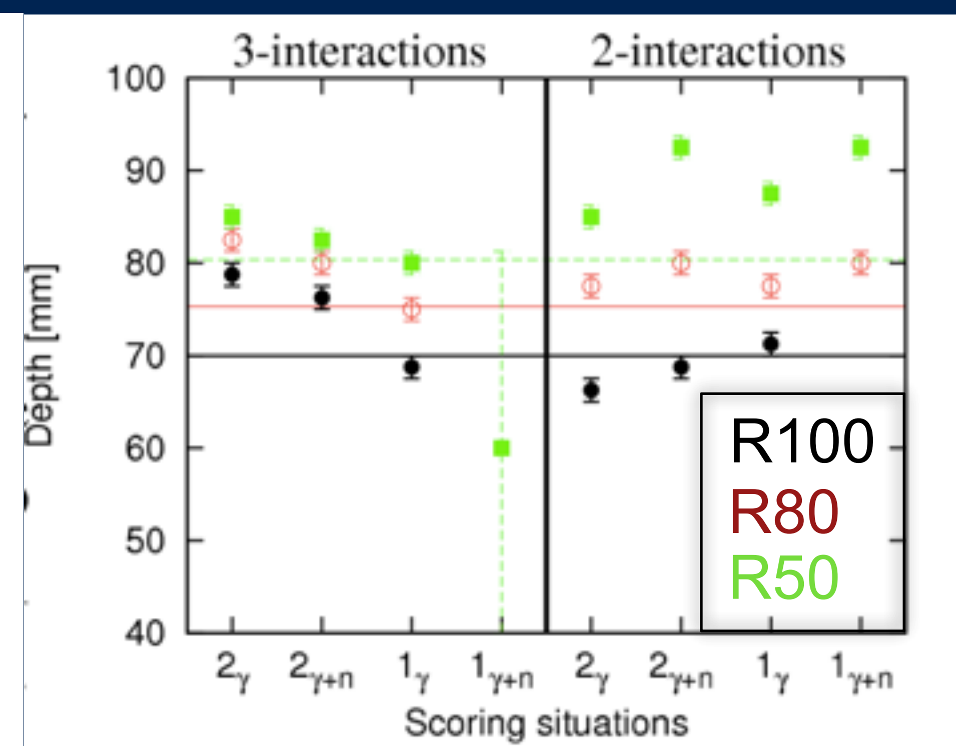
Neutron rate

E(MeV)	$R_n(10^8 p/s)$
100	*0.2995*
140	*1.1975*
180	*3.1947*

100 MeV



180 MeV

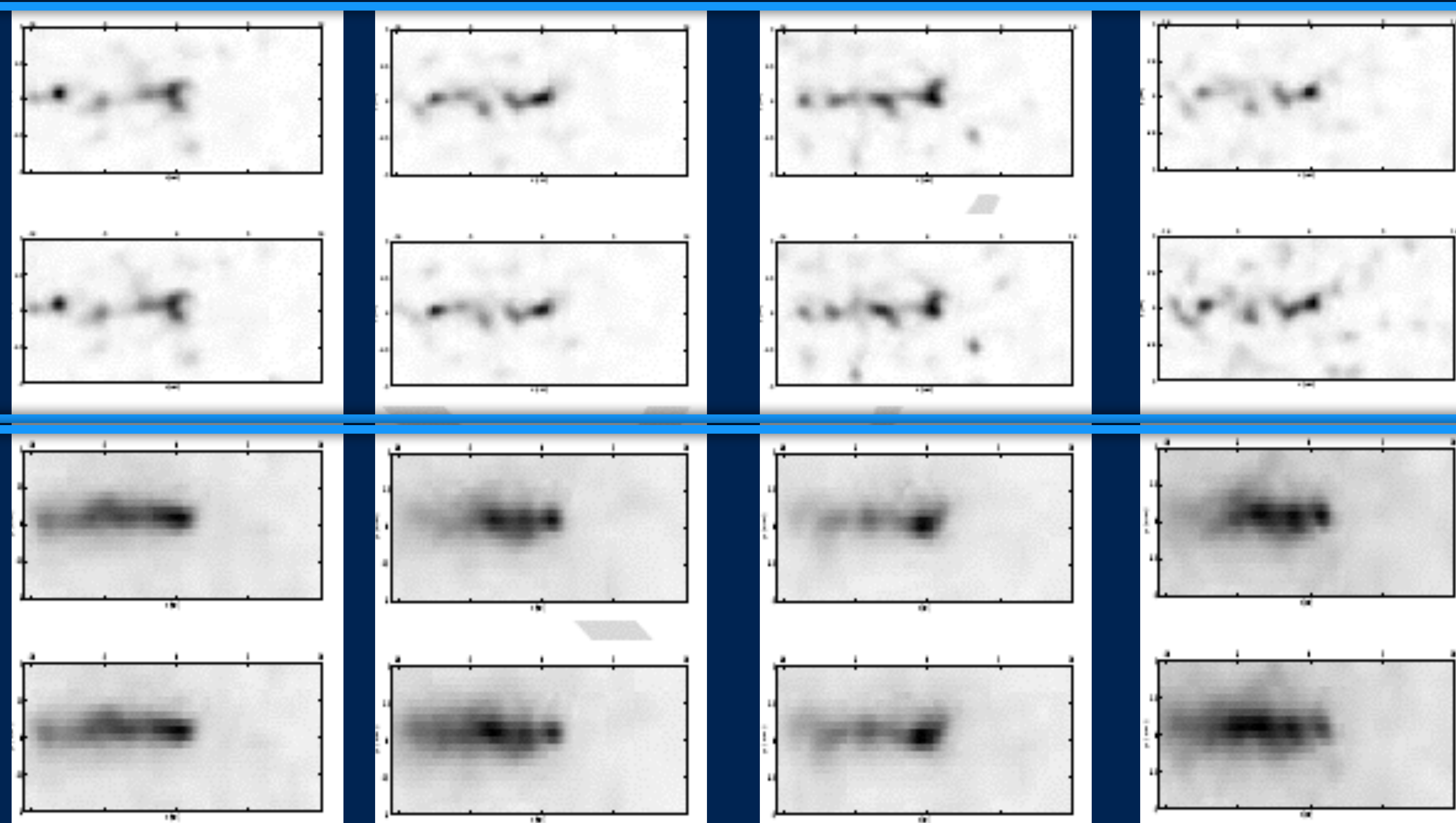


T_W = 0.75 ns

Reconstructed images with neutrons and random events

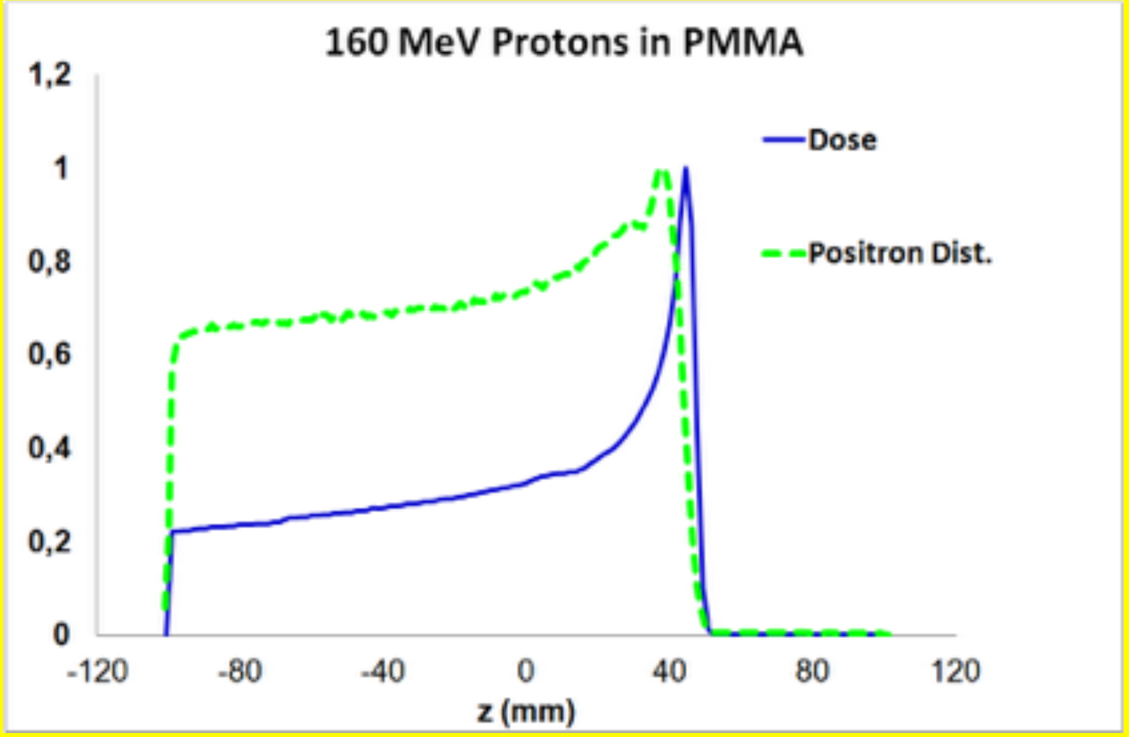
2-int. and 3-int reconstructed images for prompt-gamma coming from140-MeV proton beam, for different data sets and time windows.

	T_w [ns]	$2C_\gamma$	$2C_{\gamma+n}$	$1C_\gamma$	$1C_{\gamma+n}$
3I	0.75				
	2				
2I	0.75				
	2				



5x1mm^2 voxel, iter. 30

Hadron-therapy monitoring



Positron emitters (^{11}C, ^{10}C, ^{15}O, ^{13}N)

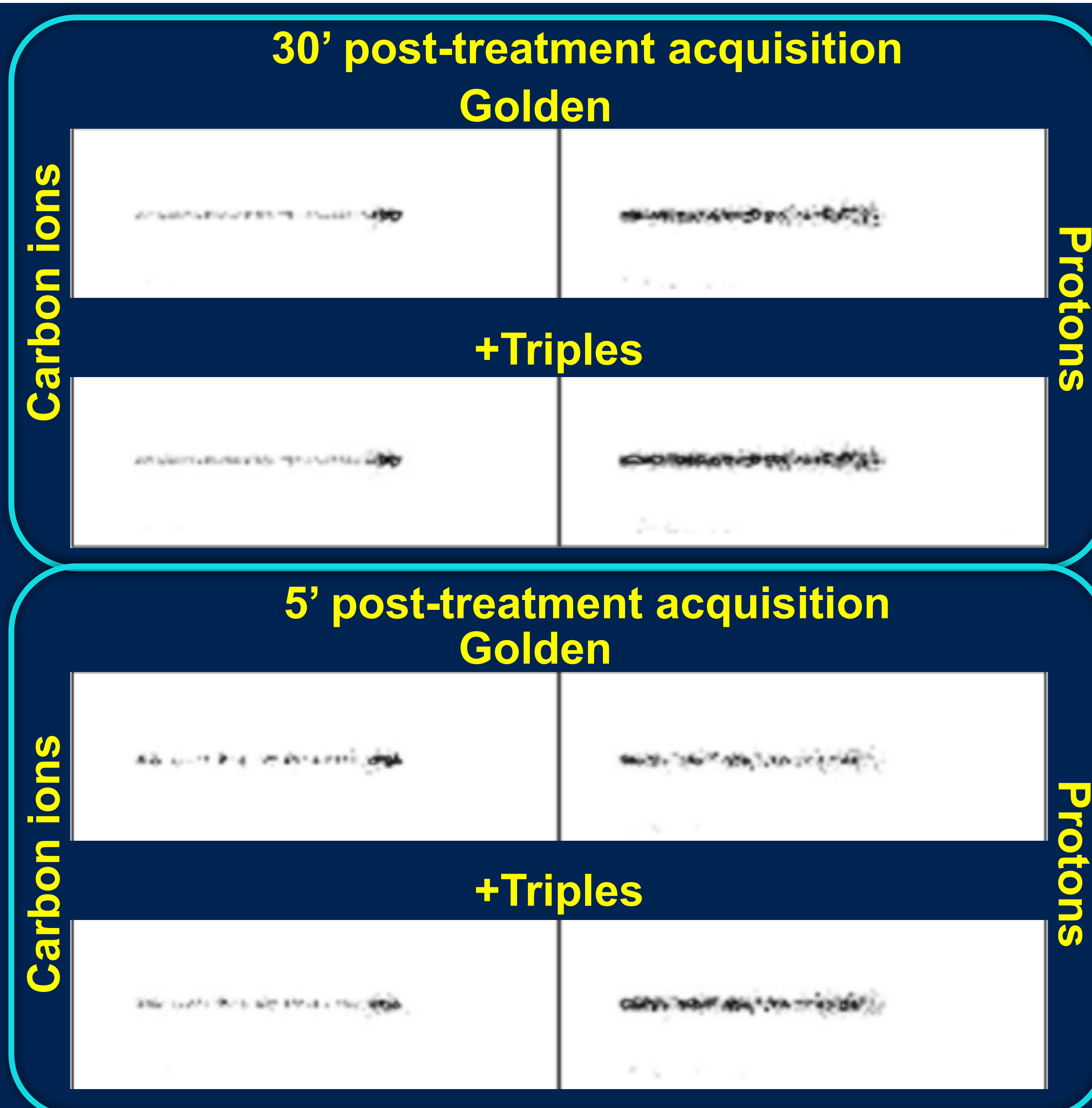
- PET imaging
- assessed technique
- low sensitivity

In-beam PET presents additional limitations given the limited acquisition time and the scanner geometry constrained by the beam delivery.

In-room PET has to deal with an even lower activity left and the physiological activity wash-out.

AX-PET for in-room PET

distal edge spread	Golden	+Triples
p 5’	4.1 mm	3.1 mm
p 30’	1.4 mm	1.0 mm
C 5’	2.7 mm	0.7 mm
C 30’	0.7 mm	0.6 mm



Conclusion

AX-PET is an extremely interesting PET device. Its potential already expressed so far in:

- providing a platform to test novel reconstruction algorithms such as **triple inclusion**.
- scalable and adaptable to different applications, such as **small animal and brain imaging**.
- **Novel scanner** configuration of AX-PET full ring is under study.

Hadron-therapy monitoring opens a number of challenges in PET and SPECT imaging.

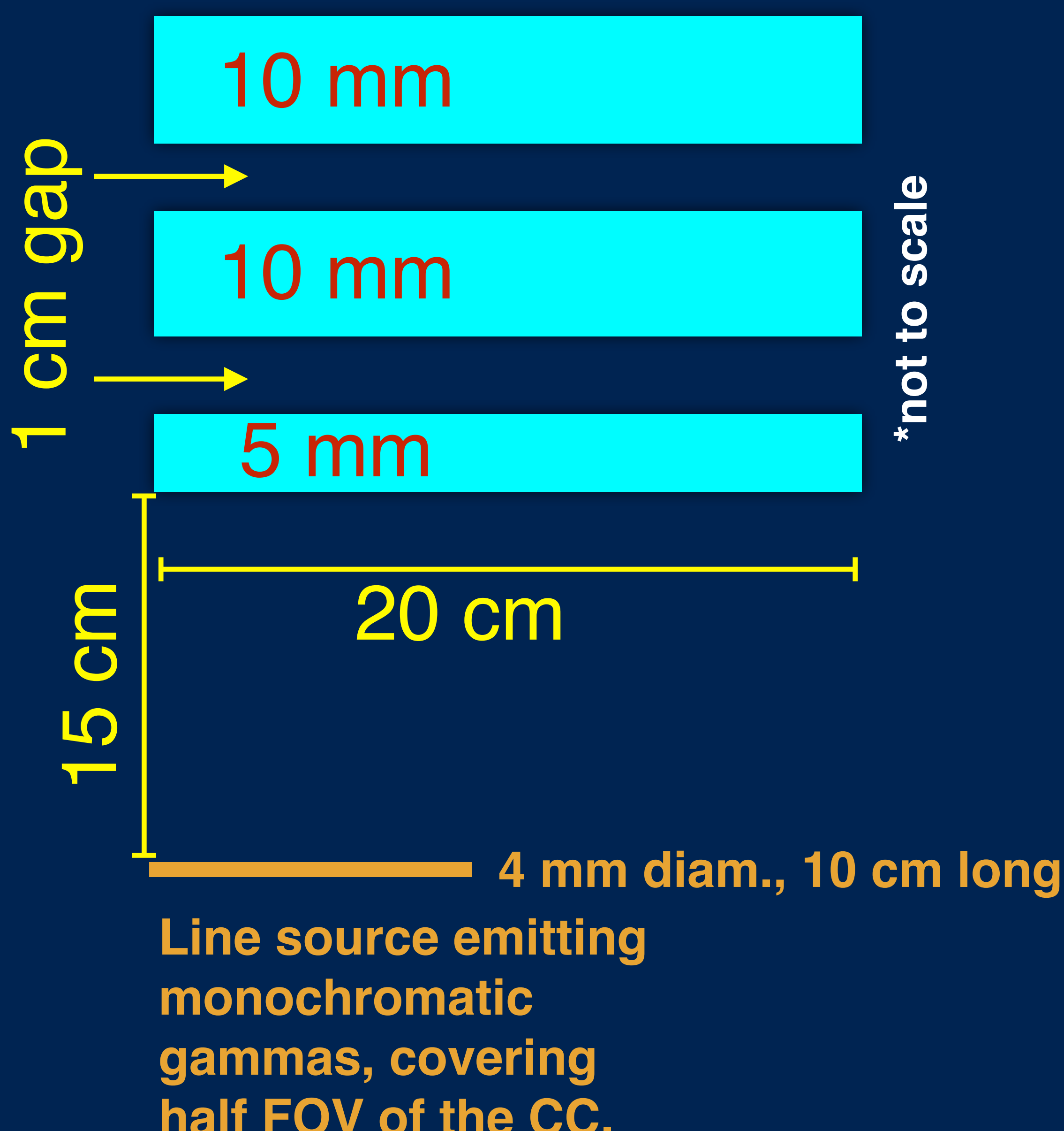
- Compton Imaging shows a potential in prompt gamma detection, but still deeper understanding is required.
- Recovery of the sensitivity in PET HT monitoring is possible via novel approaches, as AX-PET triple inclusion.


Merci beaucoup!

Back-up slides

Compton Telescope based on monolithic crystals

A three layer Compton Telescope, based on LaBr crystals, has been simulated.



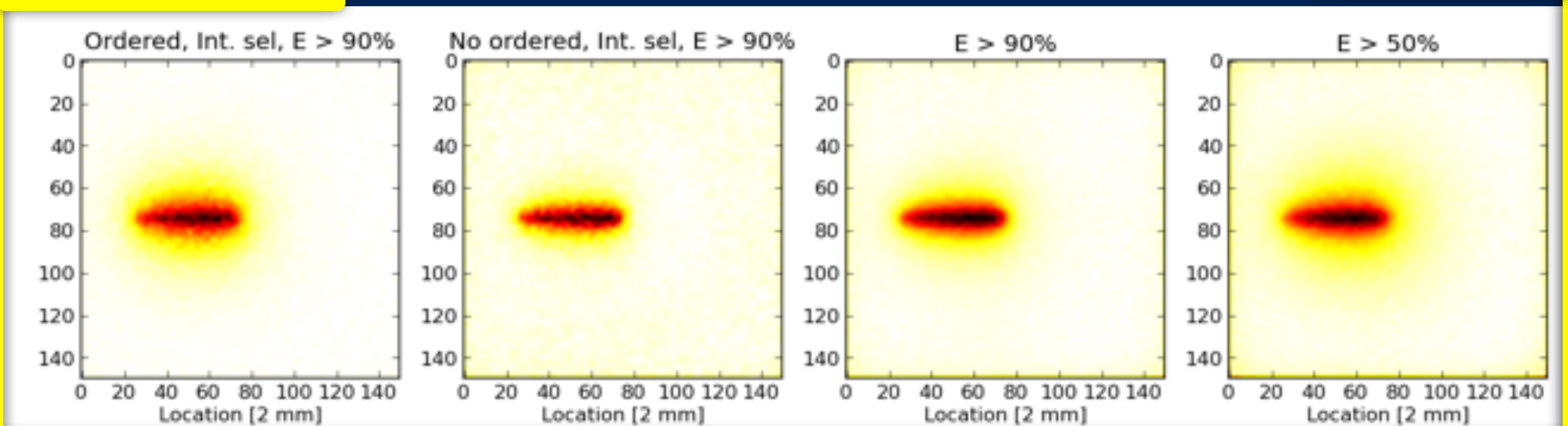
- Simulation tool: **GATE**, modified to track Compton and Photoelectric interactions within the crystals.
  - No electronics readout modeled, eventID selection of the coincidences. $E_{FWHM,\ 511\ keV}=7\%$
- Events are selected by different **"purity" filters**:
  - **Energy filter**: 90% of the initial gamma energy is deposited. Otherwise, 1 MeV minimum threshold is applied.
  - **Interaction filter**:
    - **3 hit layers** (3L) require 1 Compton or Photoelectric interaction per crystal.
    - **2 hit layers** (2L) require 1 Compton + 1 Photoelectric
  - **Ordering**: hit layers are ordered by the time stamp provided by the simulation (no time blurring applied)

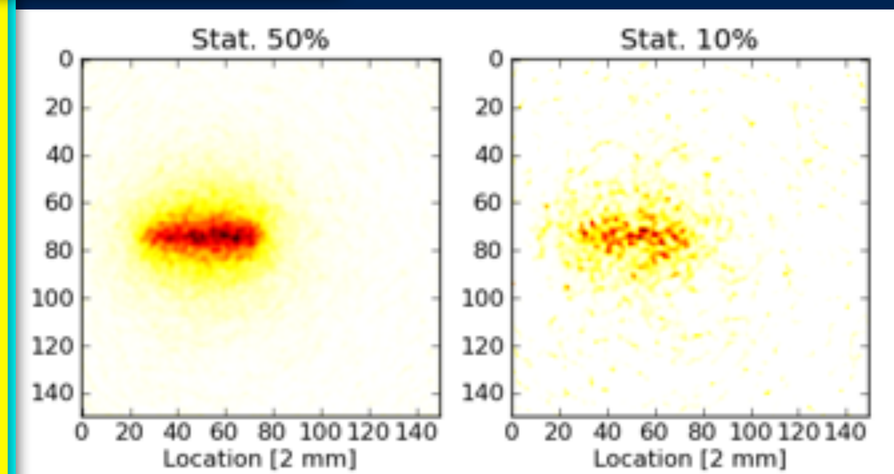
Coincidence filtering

- Detected coincidences with 2 and 3 hit layers are selected and processed through different selection filters.

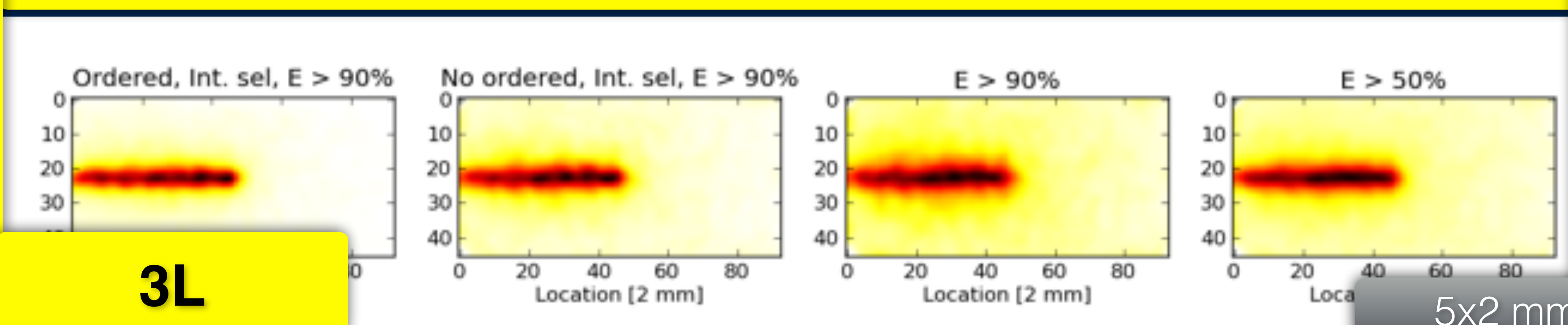
2L

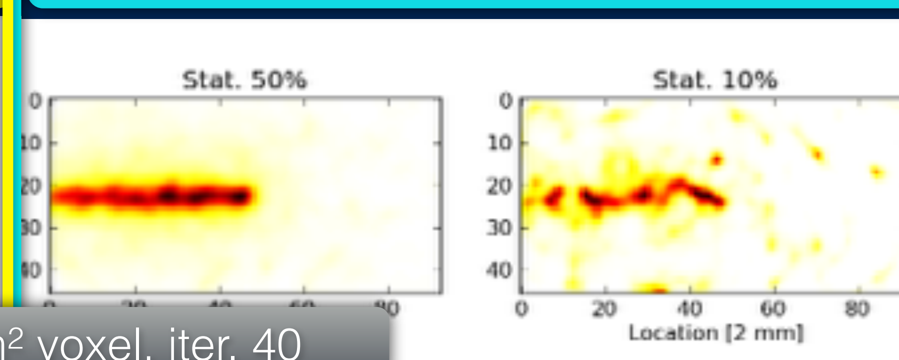
2x2 mm^2 voxel, iter. 20





780k		197k	8k
High selection →	Low selection	Smaller statistics	
220k		55k	2k



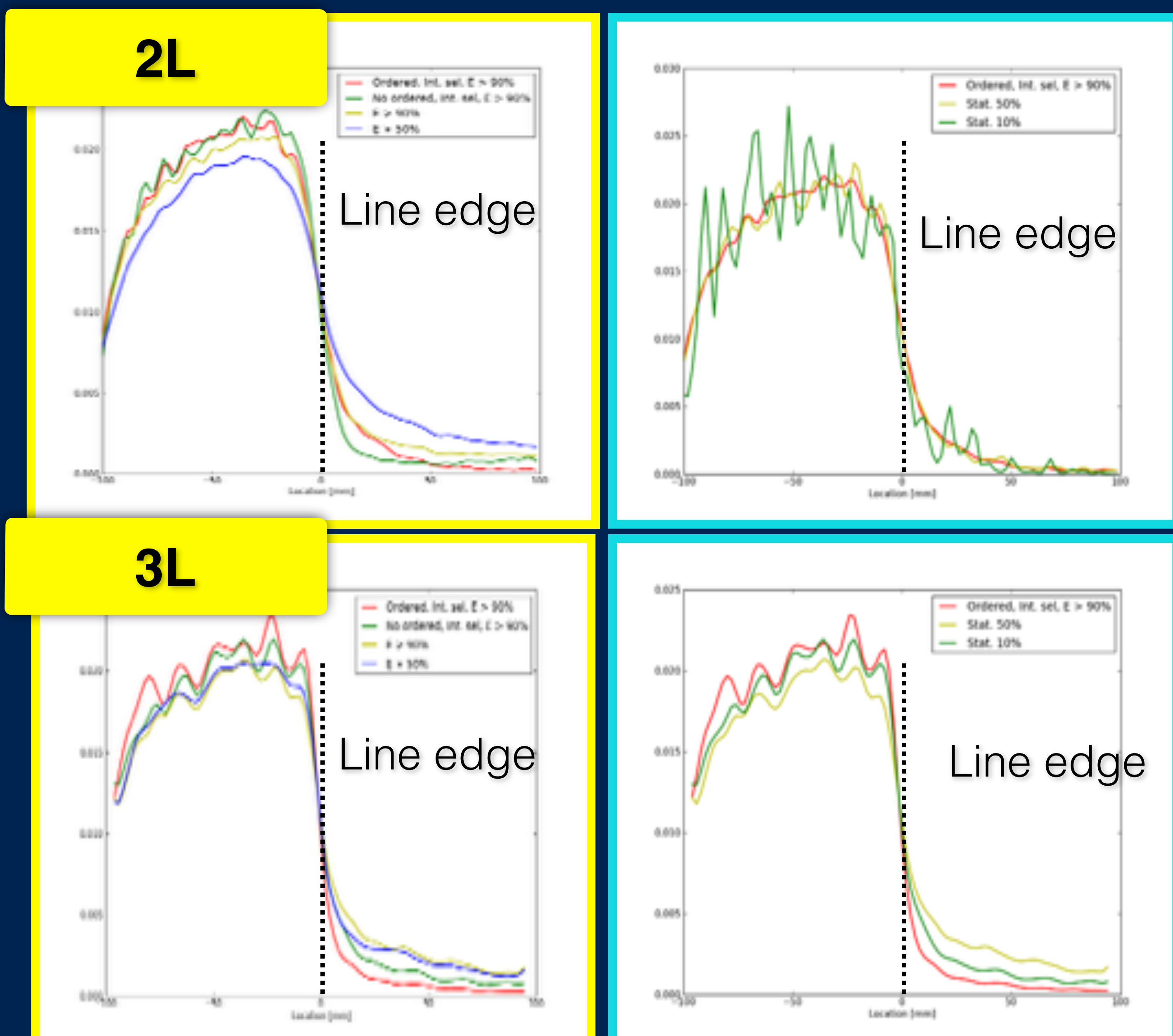


3L

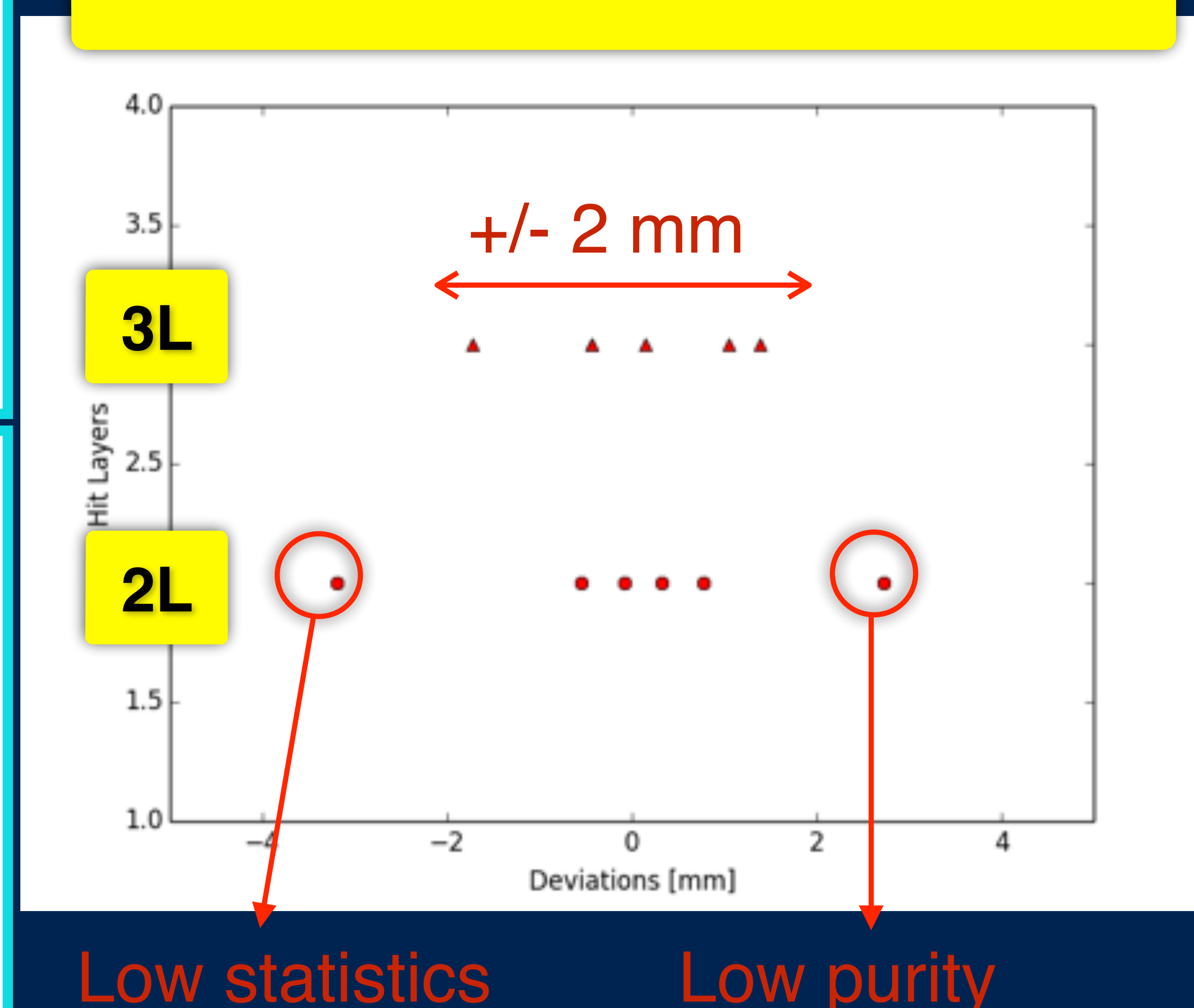
5x2 mm^2 voxel, iter. 40

Line edge location

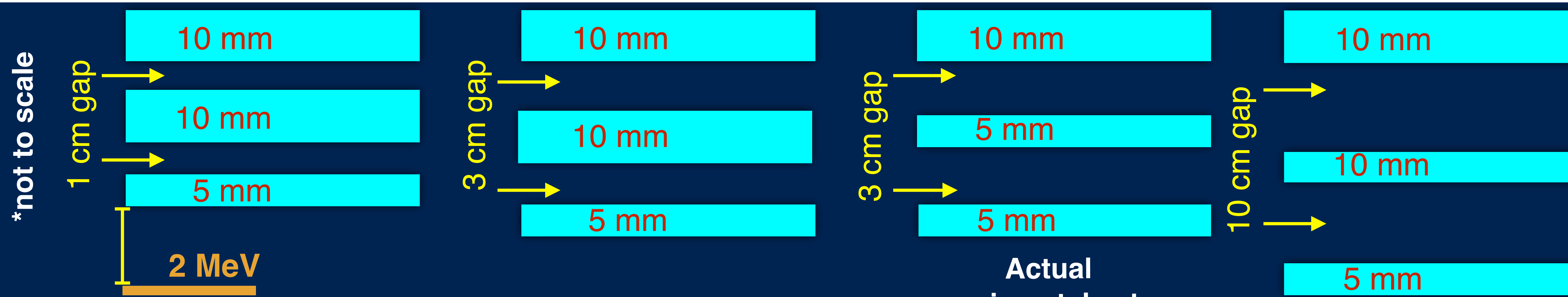
The accuracy in locating the line source edge is not strongly affected by the event selection and statistical abundance.



Line source **edge spread** over different reconstructed samples (R98)



Geometrical impact



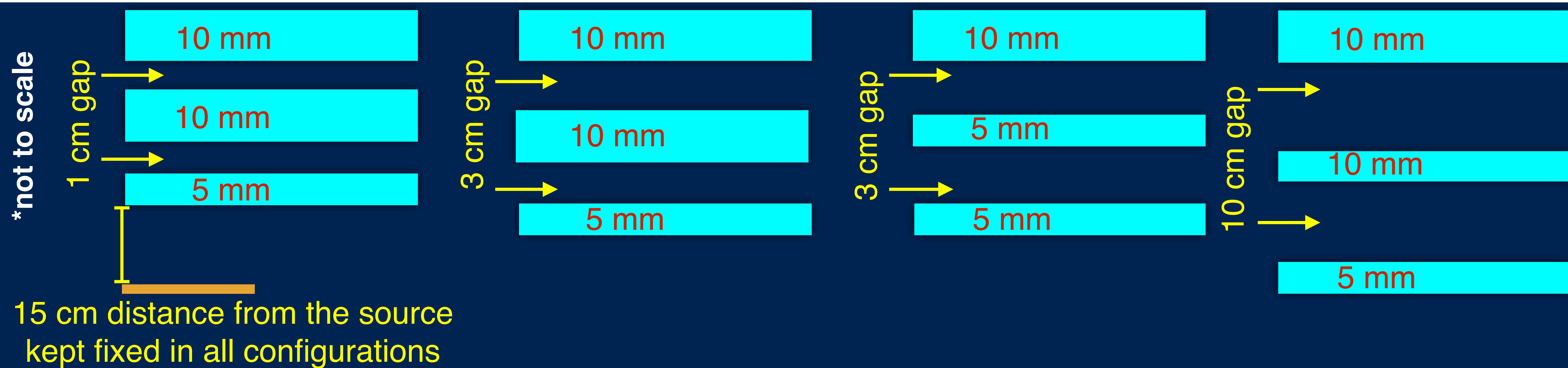
15 cm distance from the source kept fixed in all configurations

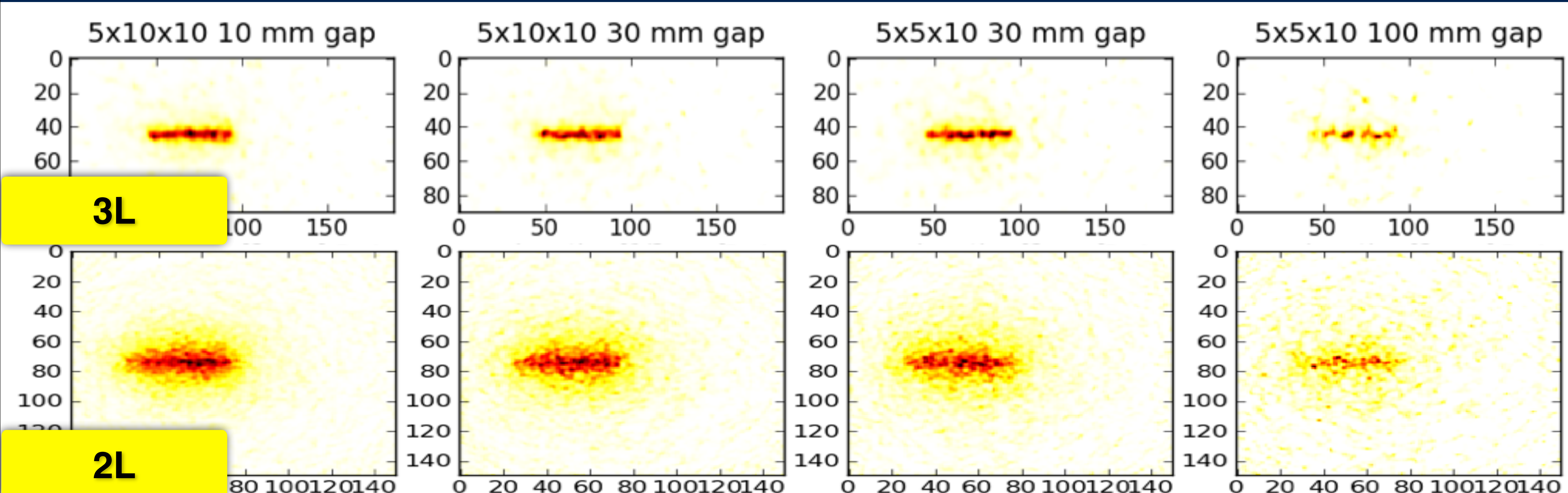
Actual experimental set-up

2L	65274	45578 **(-31%)**	37563 **(-43%)**	13555 **(-80%)**
3L	19437	10285 **(-48%)**	9347 **(-52%)**	1627 **(-92%)**

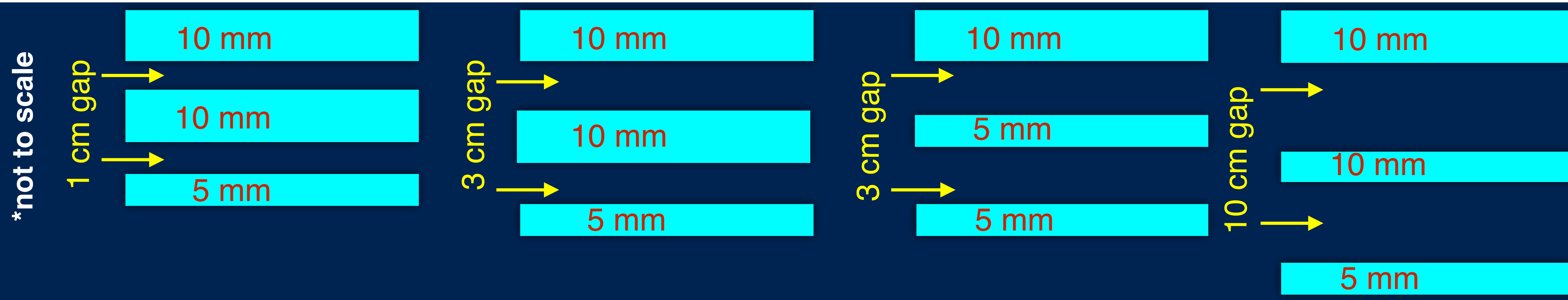
*E>1 MeV, Interaction Selected and ordered

Geometrical impact

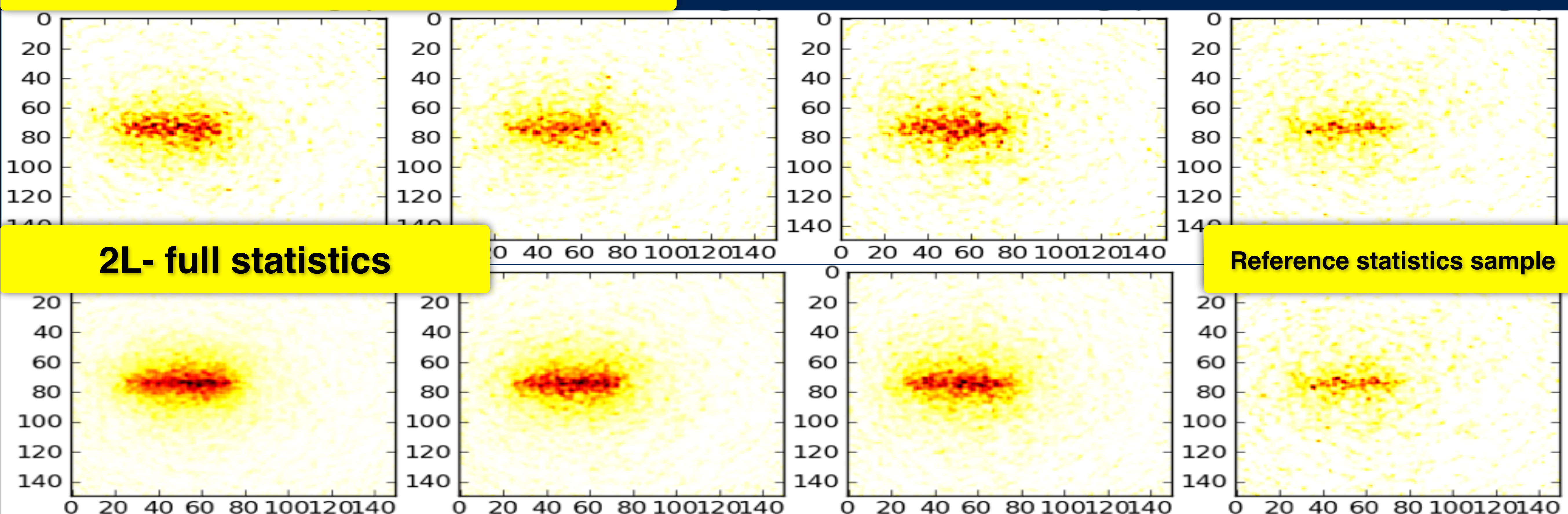




Geometrical impact



2L - same statistics ~14k as



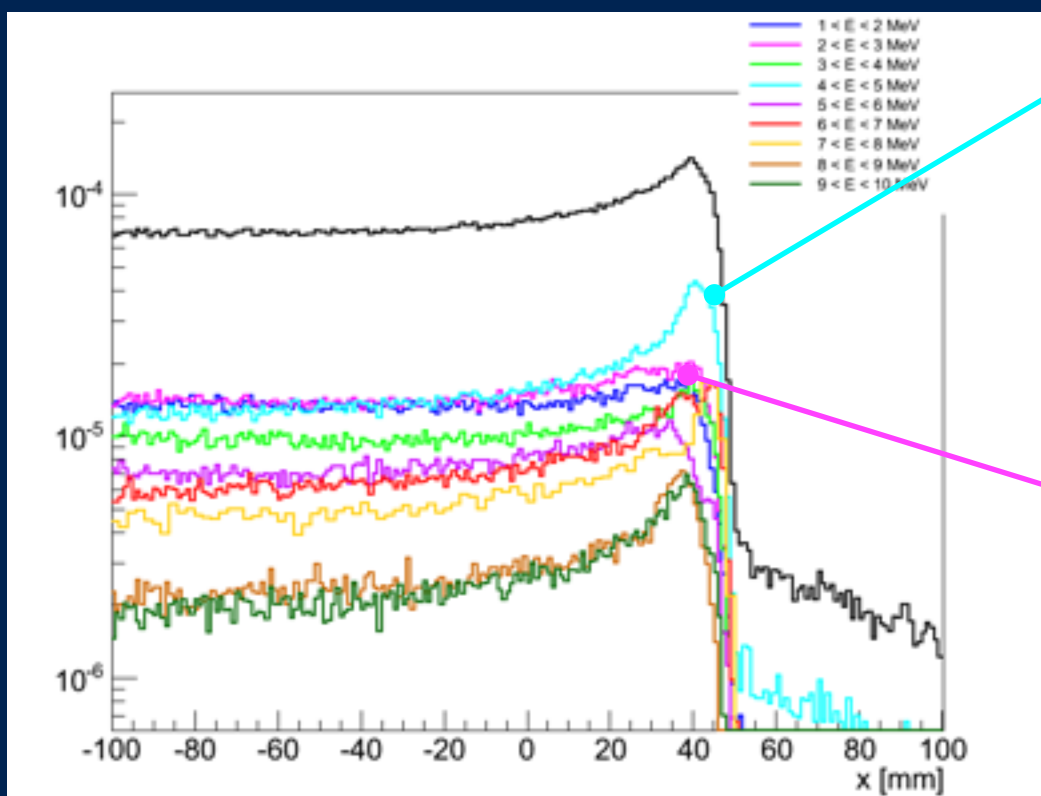
2L- full statistics

Reference statistics sample

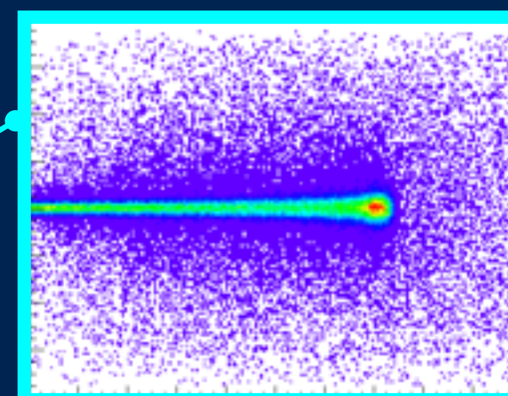
Prompt gammas energy spectrum

In case of proton beams, an average of **0.3 prompt gammas per proton** is expected.

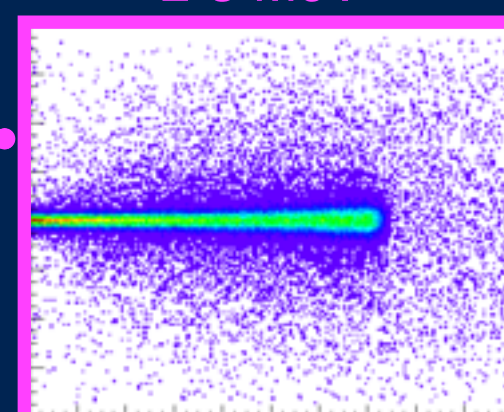
The spectrum can extend up to 20 MeV, but most abundant flux is from the **2-7 MeV energy** range.



4-5 MeV

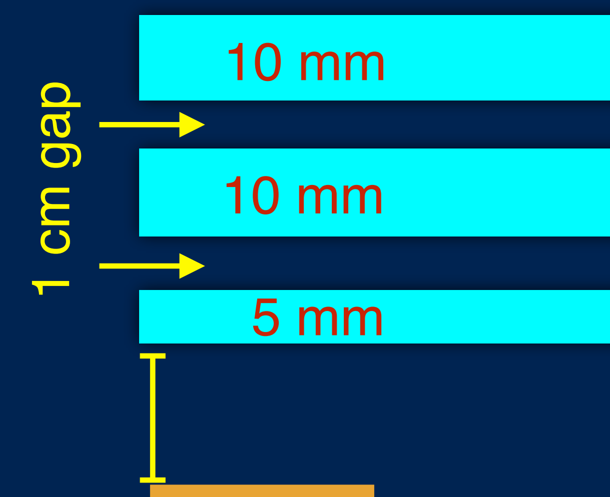


2-3 MeV

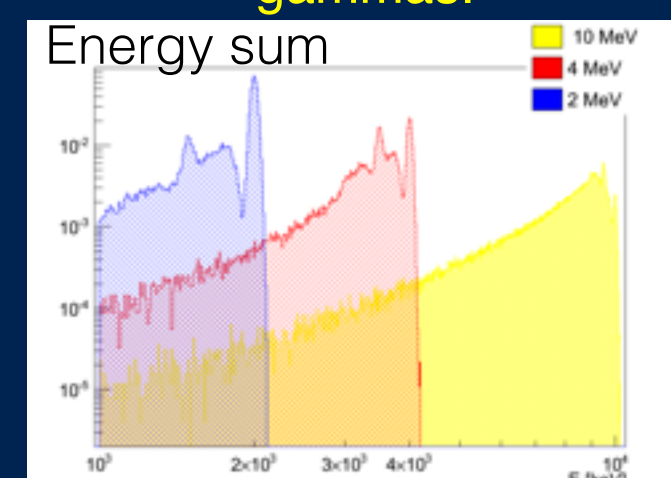


Prompt gammas vertex distribution from a 160 MeV proton beam in PMMA (Geant4 QGSP-BIC-HP) selected for different exiting energy ranges.

Investigating the impact on the final image of the energy of the incoming gamma.

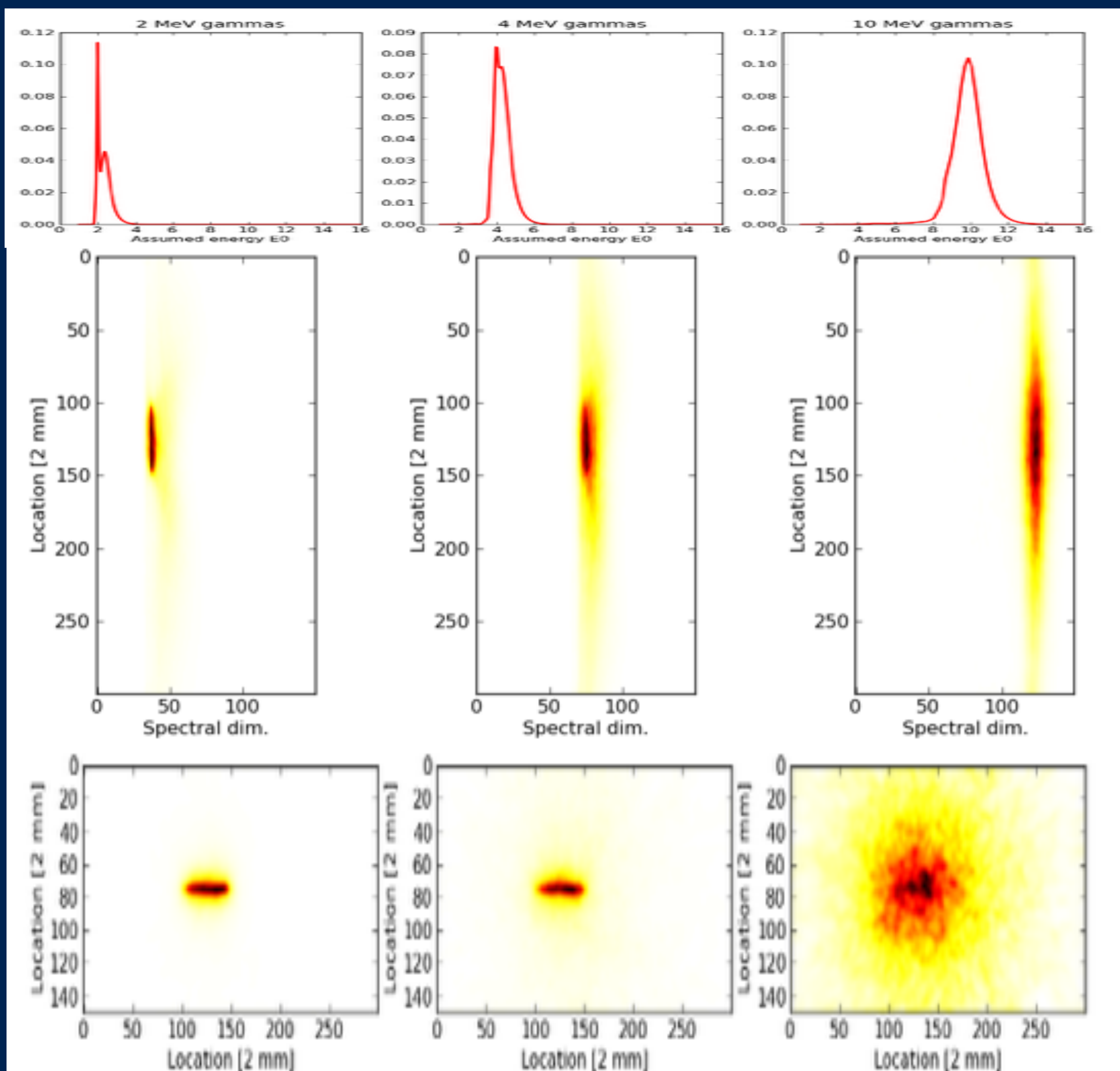


Monochromatic source emitting 2, 4 and 10 MeV gammas.



Gamma energy impact on Compton image

2 MeV | 4 MeV | 10 MeV



- **Low 1 MeV threshold** applied to the energy sum.
- **No filters** applied.
- **Spectral reconstruction of 2L** events is performed over a wide energy spectrum: 1 to 16 MeV.

- Energy increase affects the image resolution, then filtering of events becomes more crucial.
  - larger fraction of pair production
  - poorer spatial resolution
  - energy deposition losses