GROUPE XENON

# Atelier pôle imagerie GDR MI2B
# Réflexion sur le défi 10 ps
*Amphithéâtre Pierre-Gilles de Gennes, Université Paris-Diderot*

# Toward a whole body XEMIS camera ? A new generation of Compton camera based on liquid xenon


**D.Thers – IMT Atlantique**


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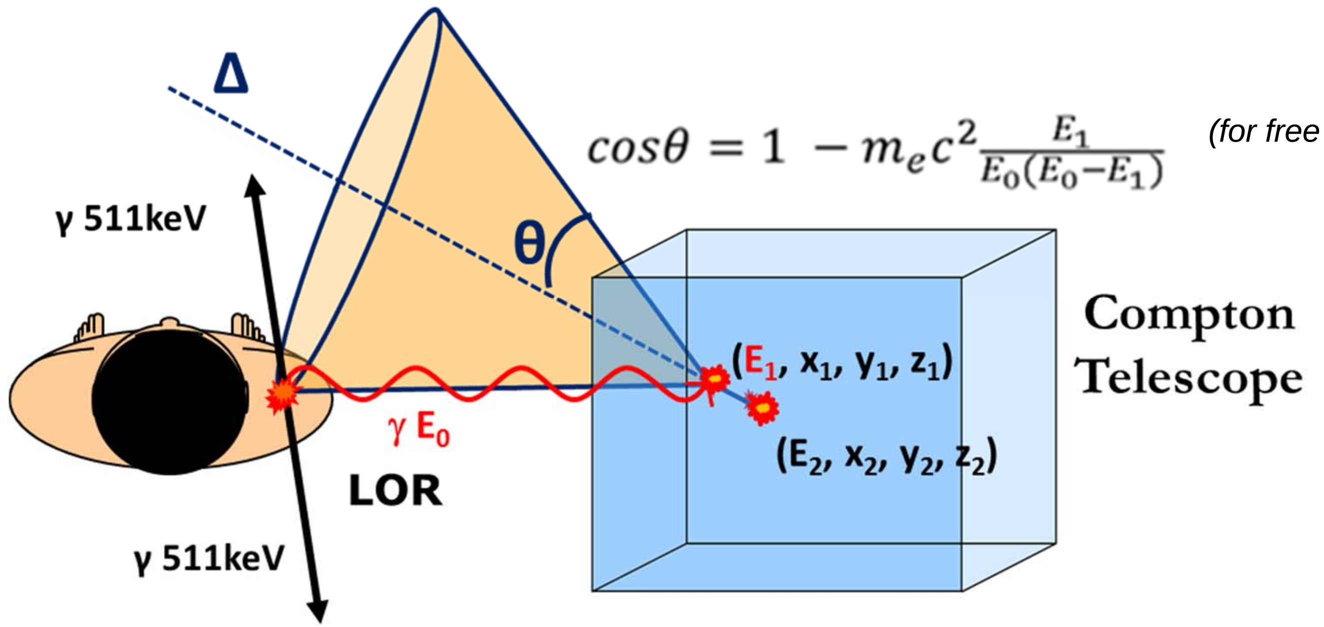
École Mines-Télécom

UNIVERSITÉ DE NANTES

June 11th 2018

# 3γ imaging : motivations




## Event per event line-cone crossing

**LOR : Line Of Response, a straight line defined by two detected points or by beam**

**Cone :Reconstructed γ direction**
- Spatial resolution ⇒ axis Δ of the cone
- Energy resolution ⇒ opening angle θ

- Direct 3D position of each decay
- Major implication for both administered activity and scan time reduction

**For which images ?**
- $^{44}Sc$ (produced by ARRONAX) radio pharmaceutics for Nuclear Medicine with XEMIS2
- also for whole body scale with new prototypes ?

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# Challenge : the future of γ imaging

New ideas mandatory for :
- from **1 to 100 Bq/ml** injected activity in nuclear medicine
- **real time (s) monitoring** in hadrontherapy

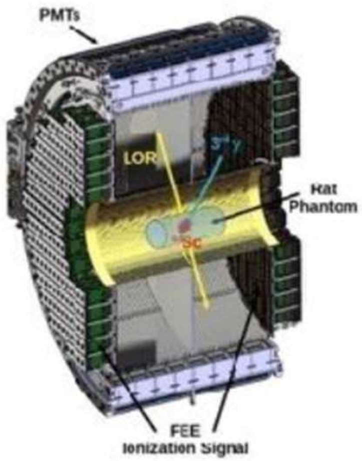
➢ Very active research, worlwide

Development of LXe technologies at Nantes with XEMIS (Xenon Medical Imaging System)

## Nuclear Medicine scaling up

| XEMIS1 | XEMIS2 | XEMIS3 |
|---|---|---|
| R&D | Small animal imaging | Whole body imaging |

**30 kg**
**12 cm drift TPC**




**200 kg**
**2 x 12 cm drift TPC**

**From 2020**

**LXe clinical camera**

- Neurology: ~250 kg
- Paediatrics: ~700-800 kg
- Whole body: few tons

And for hadron therapy ?

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# Price to pay : it works with natural xenon

Xenon is only extracted from atmosphere : ~ 40 billion of tons at ~ 0.087 ppm concentration

- Big Air Separation Unit :
  - 1 ton/year of xenon where ~ $2.10^5$ tons of liquid oxygen are produced
- World production : 60-70 t/year
- cost : 0,5 - 4 k€/kg, mostly due to electricity consumption for initial separations

Strong constrains for an industrial application in medical imaging:
- The world production will have to be increased in case of liquid xenon camera "rush"
- Xenon procurement should be considered as long term investment/heritage !

Research projects have to trig also these issues:
- Gaseous companies: new markets, new needs mean lower price (but very difficult before the rush).
- Xenon handling processes (cryogenics) are essential parts of the work ! The camera cannot lose xenon, xenon procurement is for generations …

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# XEMIS2 : compact xenon handling

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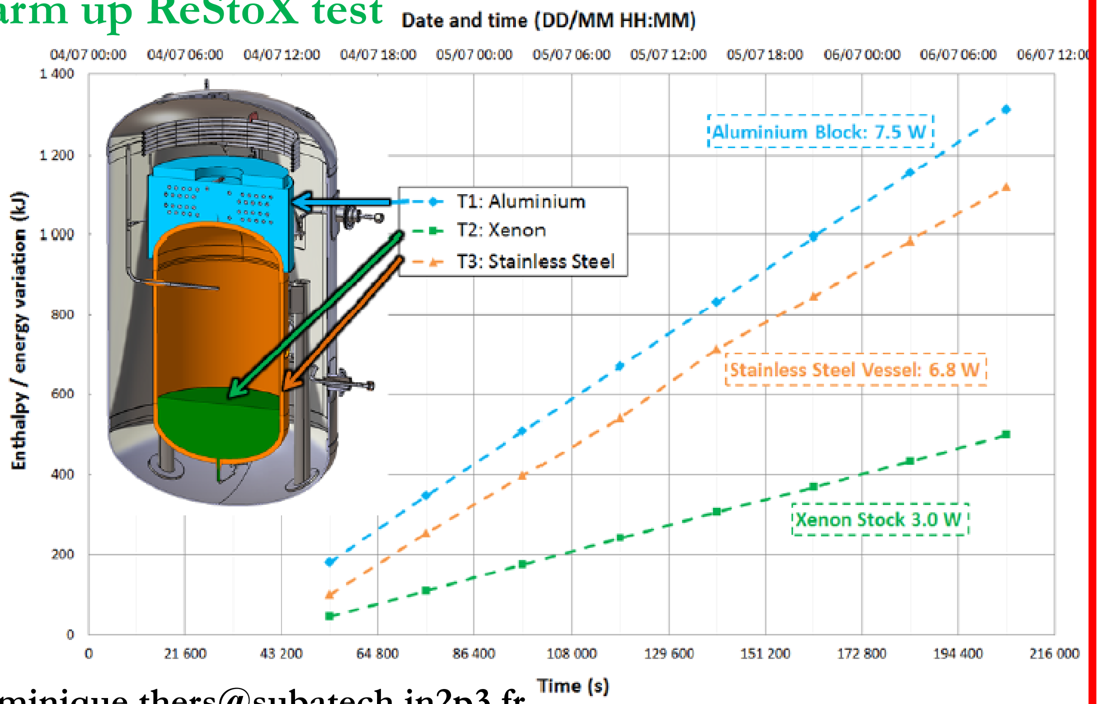
Purification Loop | ReStoX | Cryostat

Purification Loop | ReStoX | Cryostat

Thanks to a scientific collaboration with :

AIR LIQUIDE

## Warm up ReStoX test




## ReStoX for XEMIS2

(Recovering and Storage of Xenon)

- Cooling with $LN_2$
- Heavy aluminium cold head
- < 20 W of heat load
- Internal Pressure [0; 70] bars
- 200 kg xenon capacity
- very compact
- ultra « safe »
- operate without human assistance
- warm-up from LXe to Room Temperature in more than 6 months !

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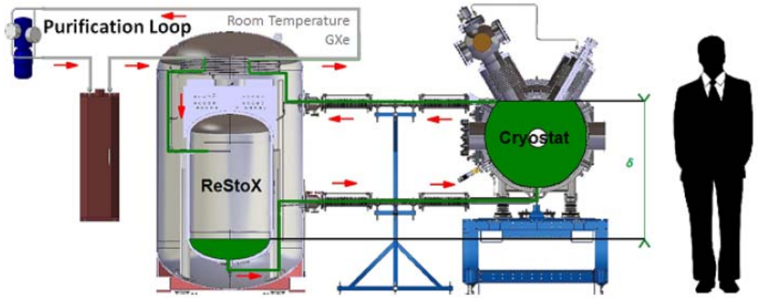
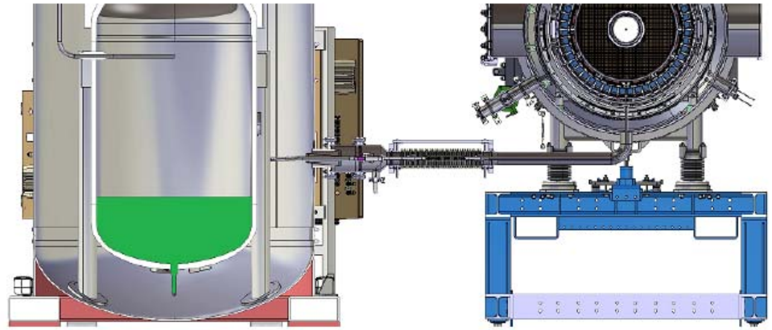
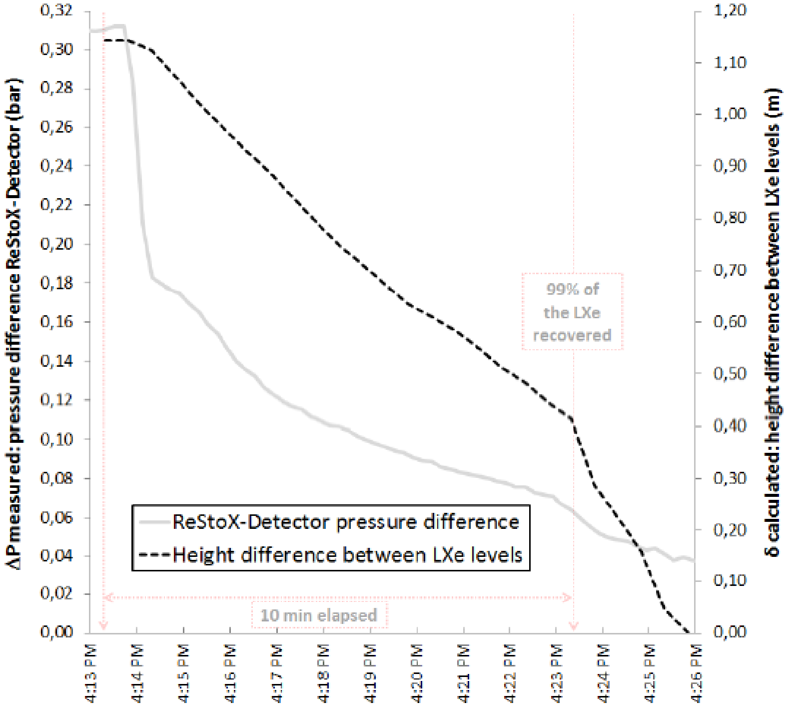
# XEMIS2 : cryogenics commissioning



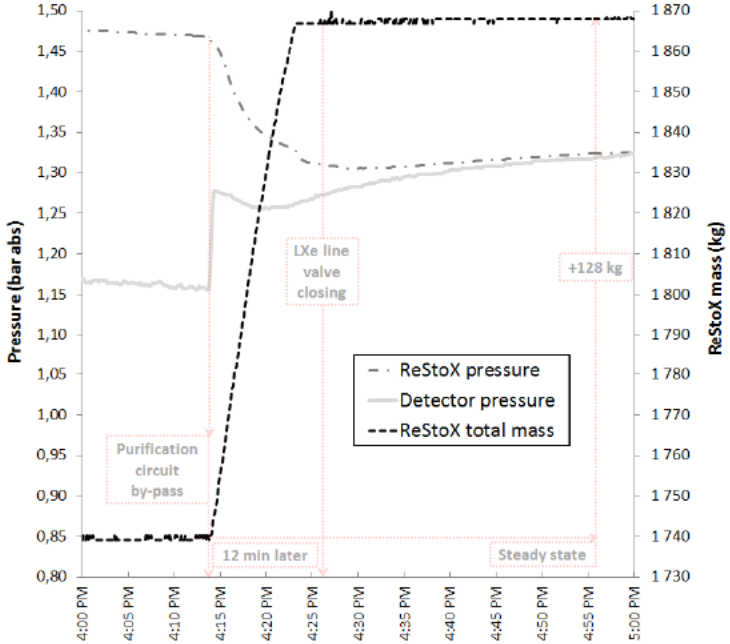

**Recovering**

Automatic if cryostat pressure increase






Less than 10 mns to recover all the xenon in the « bottle »




Ultra fast recovering assisted by gravity already commissioned
No human assistance
ReStoX is part of the closed loop, xenon is passing through it continuously

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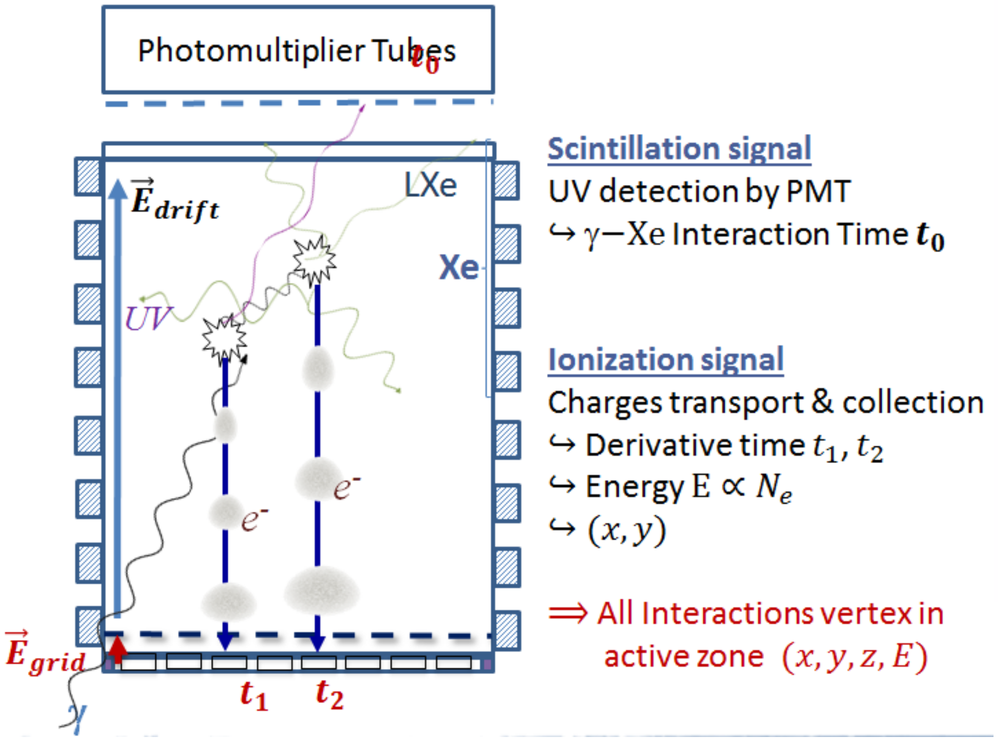
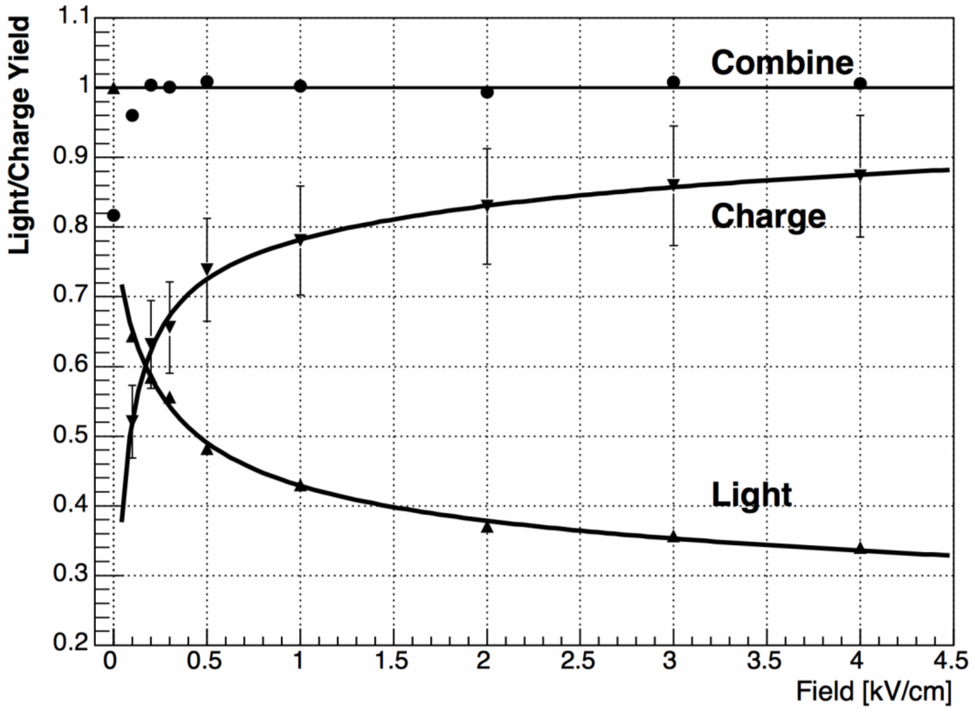
# XEMIS, Compton imaging with charge and position of electron recoils measurement






*From E. Aprile et al., "Observation of Anti-correlation between Scintillation and Ionization for MeV Gamma-Rays in Liquid Xenon," Physical Review B, vol. 76, 2007.*

**LXe TPC can resolve most of the Compton vertices and provide a dense target for high efficiency γ camera**

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# XEMIS2 : cryostat and detailed design

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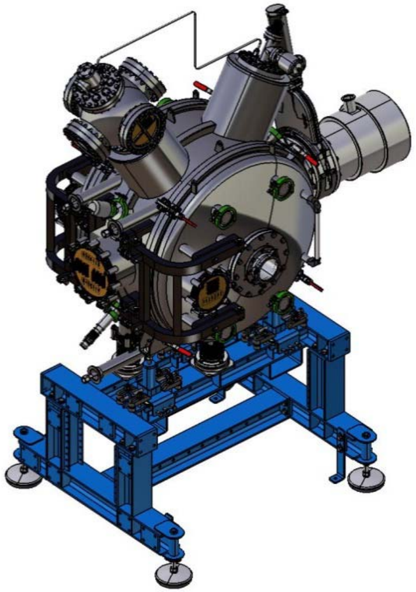
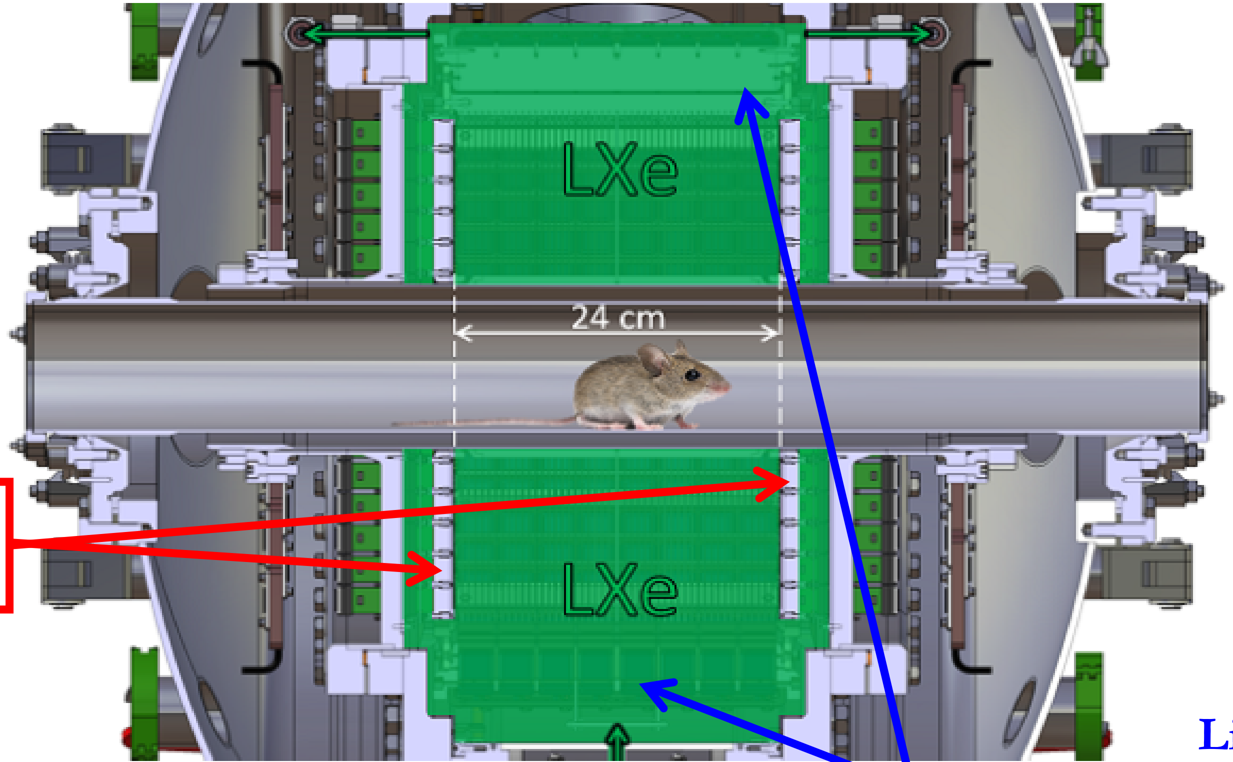
**Active volume**
- axial : 2 x 12 cm
- depth : 12 cm
- $r_{min}$ : 7 cm



**Charge read-out**

2 x $10^4$ pixels in LXe
3.1x3.1 $mm^2$ pitch

**Completely specifics**




**Light read-out**

**64 x 1x1" photo-detectors in LXE, Hamamatsu PMT**
**limited by the budget, while the ideal configuration is 8x48 x 1" photo-detectors**

Axial drift of the charges
Radial detection of the light
Best solution for small animal scale, fruitful discussions with KEK (Tauchi, Mihara) TXePET

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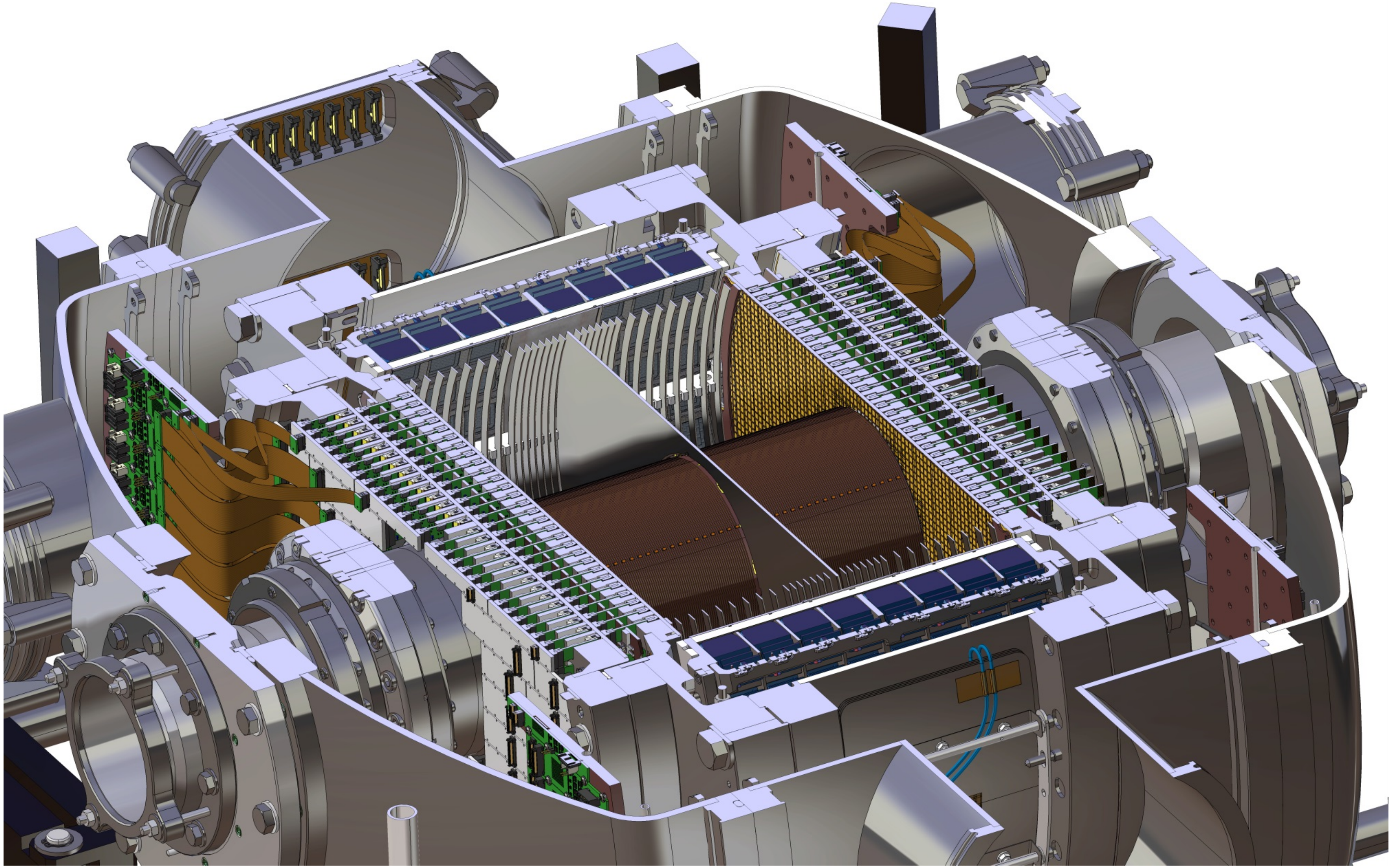
# XEMIS2 : the largest Compton telescop with LXE never built

pôle imagerie défi 10 ps



It is a challenge ! Specially designed for very low activity sensibility

# XEMIS2 : LXe performances fully simulated with Geant4, detailed design validated with MCs

Thanks to a scientific collaboration with :

## « RAT PHANTOM »

**Geometry :**
- Cylinder :
  - $r_C$ = 2.6 cm
  - l = 12 cm
- Sphere:
  - $r_S$ = 5 mm

**Material :**
- Water
- $^{44}Sc$

**Radio-Activity :**
- Total = 20,0 kBq
- Bkg (cylinder) = 19,5 kBq
- Src (sphere) = 0,5 kBq
  - Uniform distribution

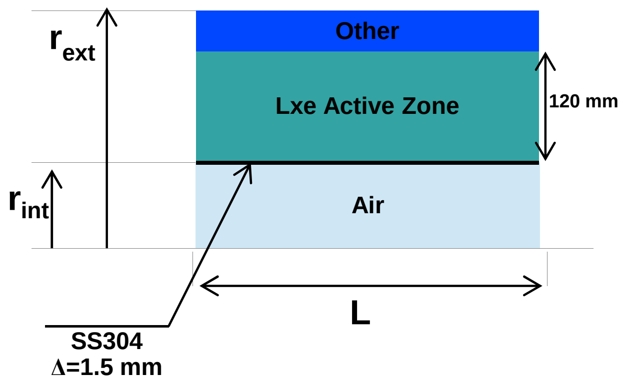
➡ **Contrast = 15**

## CAMERA

**Geometry :**
- Uniform Tube of LXe
  - $r_{int}$ = 7 cm
  - $r_{ext}$ = 19 cm
  - L = 24 cm

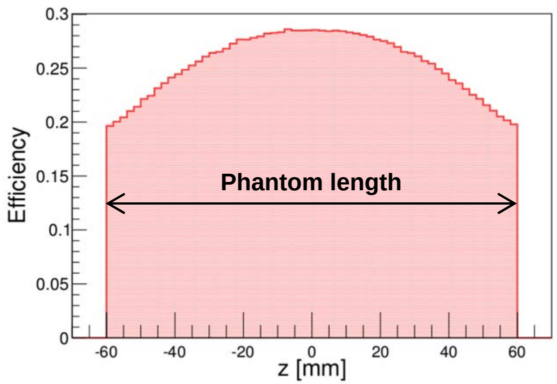
**Material :**
- Liquid Xenon

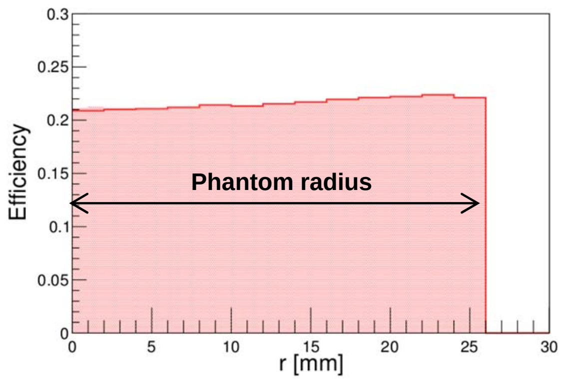
**Acquisition time :**
- $t_A$ = 20 min




## Detectable Event Fraction

At least 4 Hits in Lxe :
- 1 for each 511 keV photons
- 2 for 1157 keV photon

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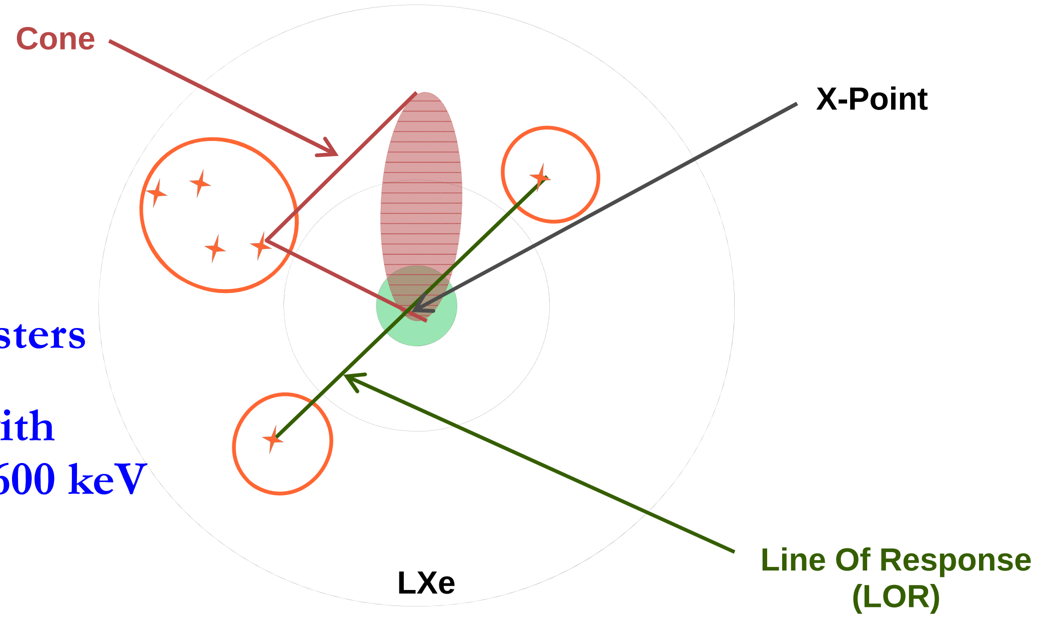
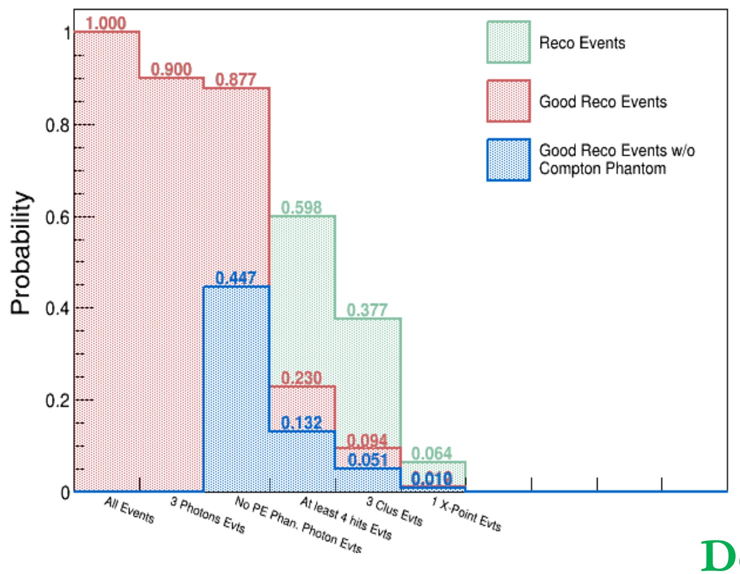
# XEMIS2 : raw line-cone algorithm developed

## Event Reconstruction Algorithm :

- All simulated evts (100 %) (a)
- At least 4 Xenon interactions (b)
- 3 Reco Groups (c) — 3 geometrical clusters
- 1 Flag (d) — 1 cone cluster with 2 interactions, $E_{tot}$>600 keV
- 1 x-point (e)




Event evolution




> 7 % expected at the end

The raw image is obtained directly
with the selected events

Debora Giovagnoli PhD thesis, work in progress

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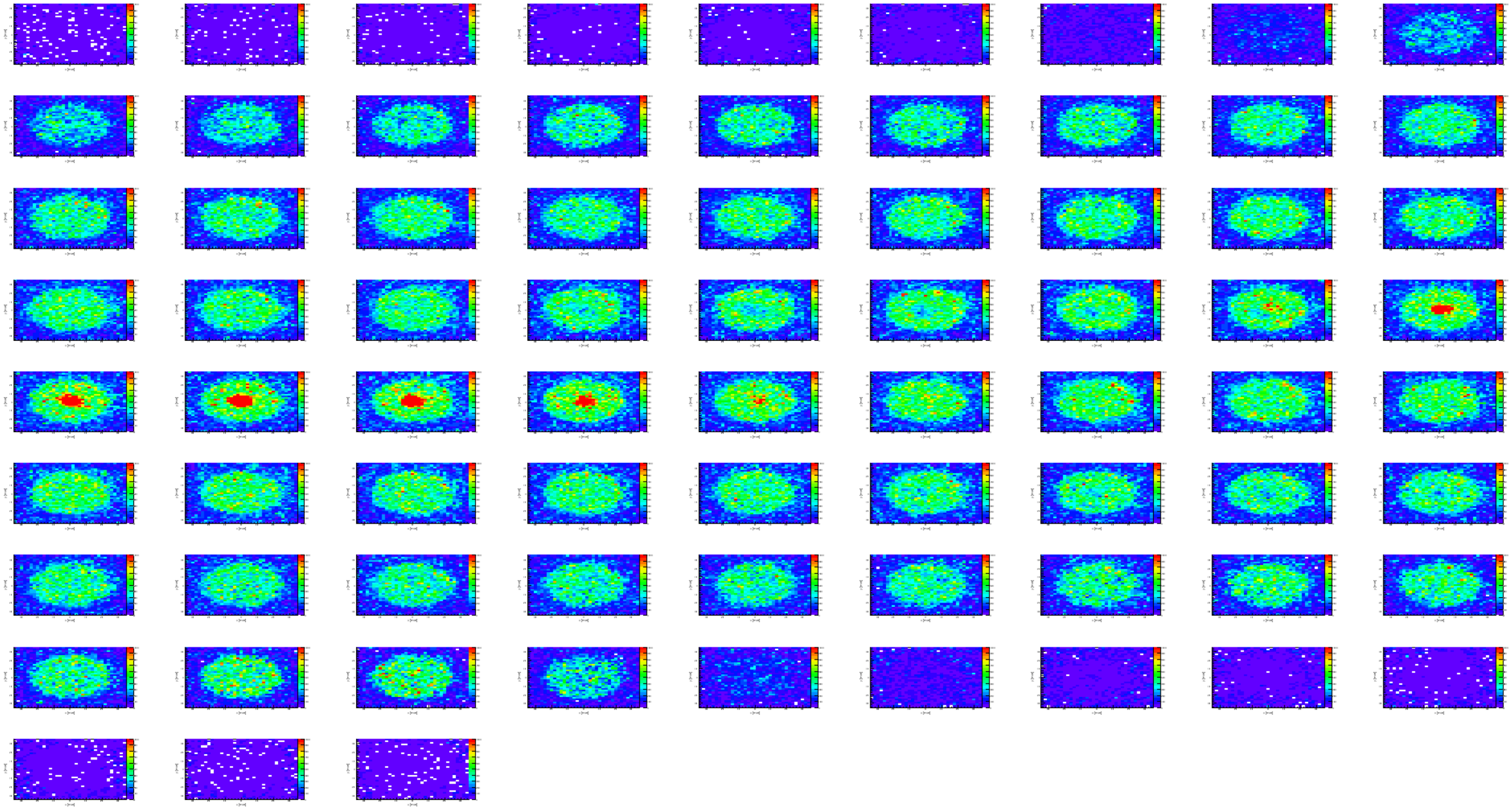
pôle imagerie défi 10 ps

# XEMIS2, expected image in 20 mns with 20 kBq

## Raw cone line Image



75 x 2 mm slices in the axial field of view
the initial contrast on the central sphere is clearly visible

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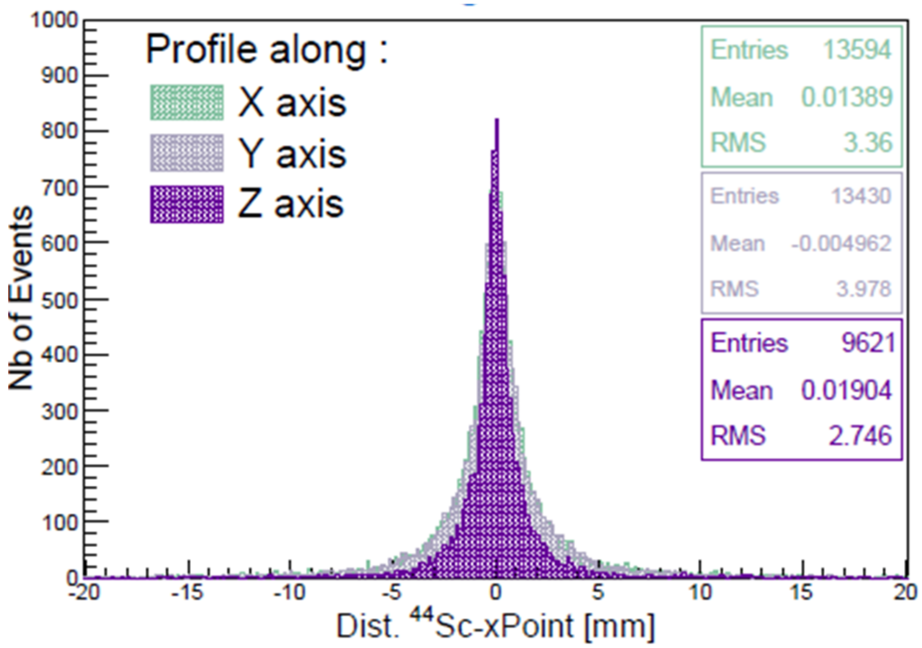
# XEMIS2, expected 3D PSF inside the FOV

Thanks to a great work of Nicolas Beaupère

Raw image : directly in the Cartesian coordinates for each crossing point
No referential transformation : absolute position in the FOV




For x, y and z :
<FWHM> ~ 1 mm
<RMS> ~ 3 mm (queue from scatter)

PSF are used for spatial deconvolution in the laboratory referential :
no projection on finite directions to manage
The dream ! easy and natural imaging technics, very small noise integrated
(only closed to the decay location)

➤ Very promising for low statistics imaging

# XEMIS2, tracking and reconstruction

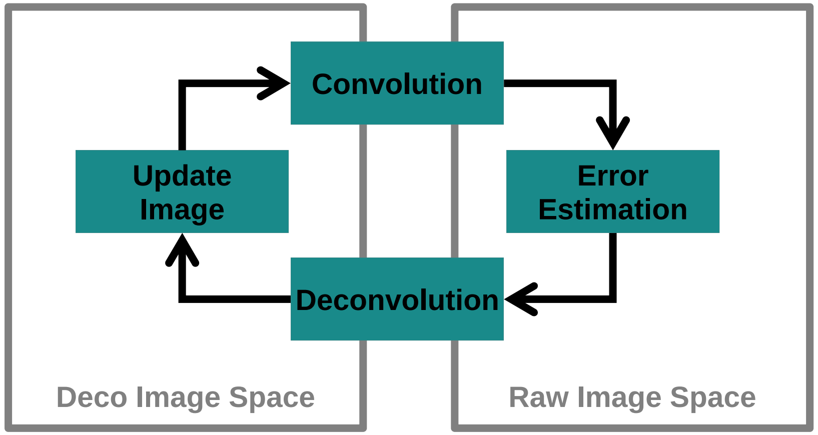
## From Raw Image to Deco Image

**Assumption : Point Spread Function uniform in all the field of view**

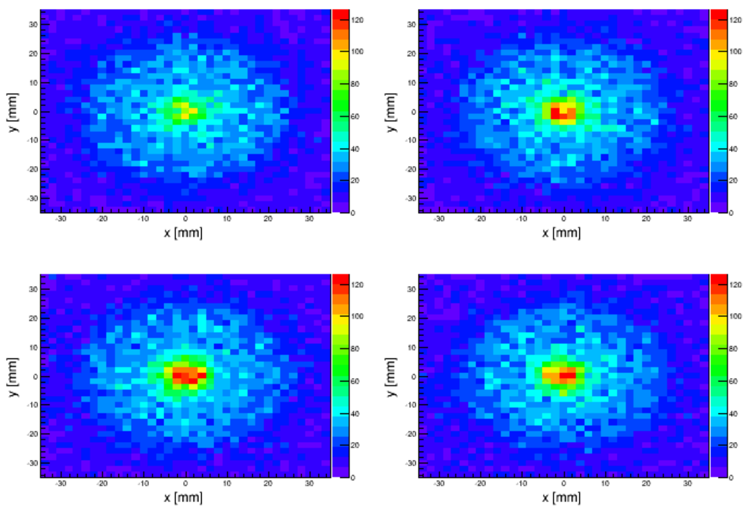
- **Idea :**
- Inverse problem of convolution
- Points image to points image

- **Algorithm :**
- Iteration 0: raw image
- Iterative Maximum Likelihood Expectation Maximization based on Poisson Distribution
- Convolution in frequency domain

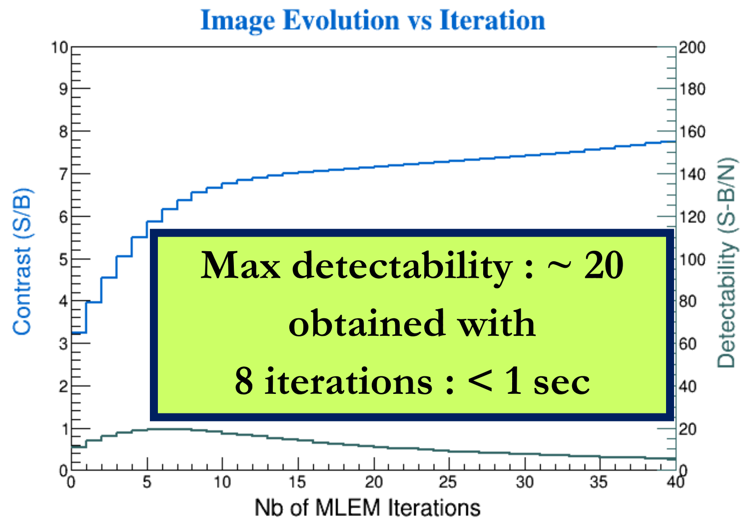
$$\lambda_i^{(n+1)} = \lambda_i^{(n)} \cdot \frac{1}{\sum_{j\varepsilon J} f_{ij}} \sum_{j\varepsilon J} \frac{p_j}{\sum_{k\varepsilon I} f_{kj} \lambda_k^{(n)}} \cdot f_{ij}$$




## Raw Image :




Deconvolution

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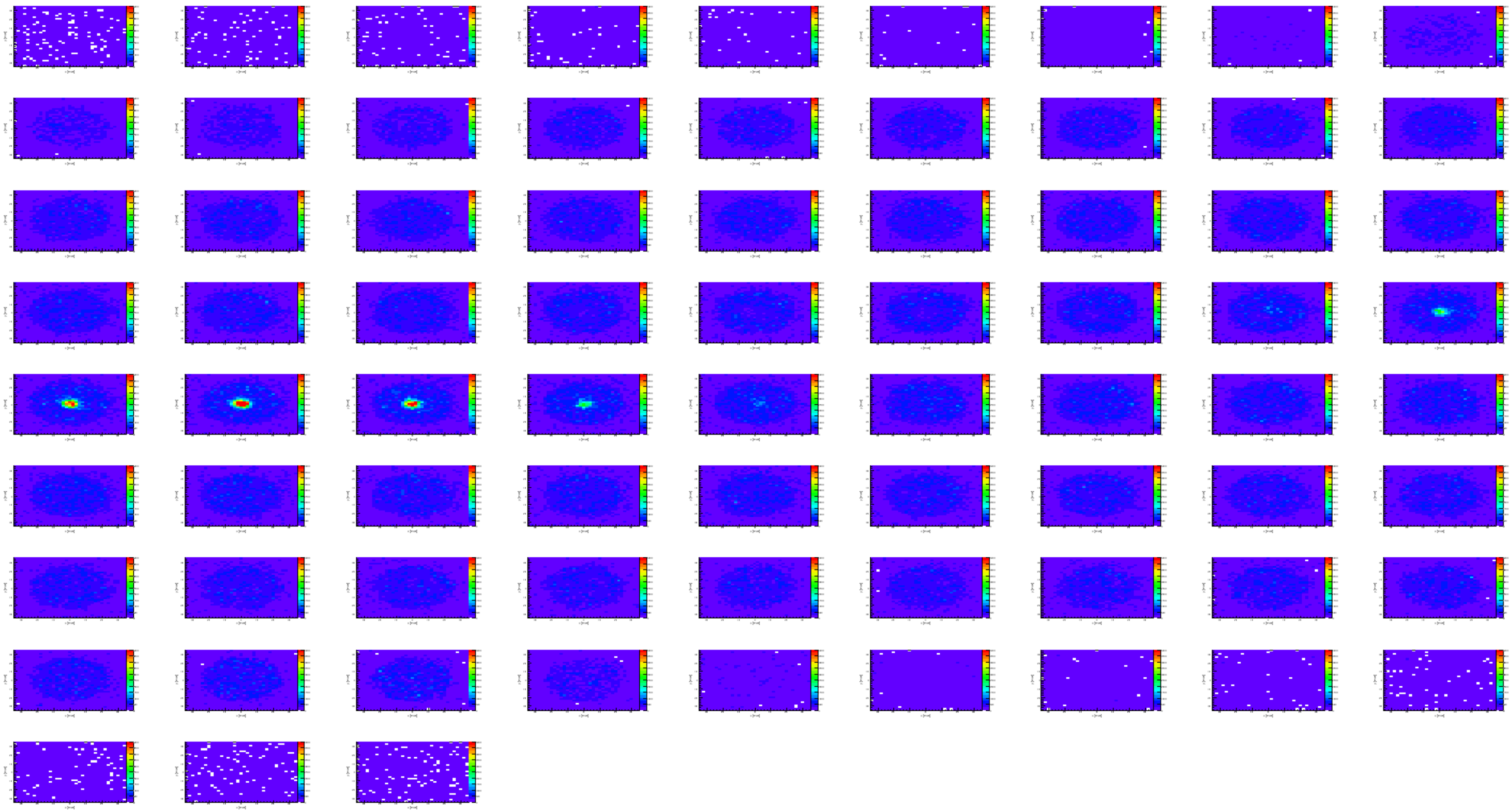
# XEMIS2, expected image in 20 mns with 20 kBq

## Deco Image



XEMIS2 adapted for 20 kBq injection
(several 100 time less than commercial μPET), work in progress for real time imaging

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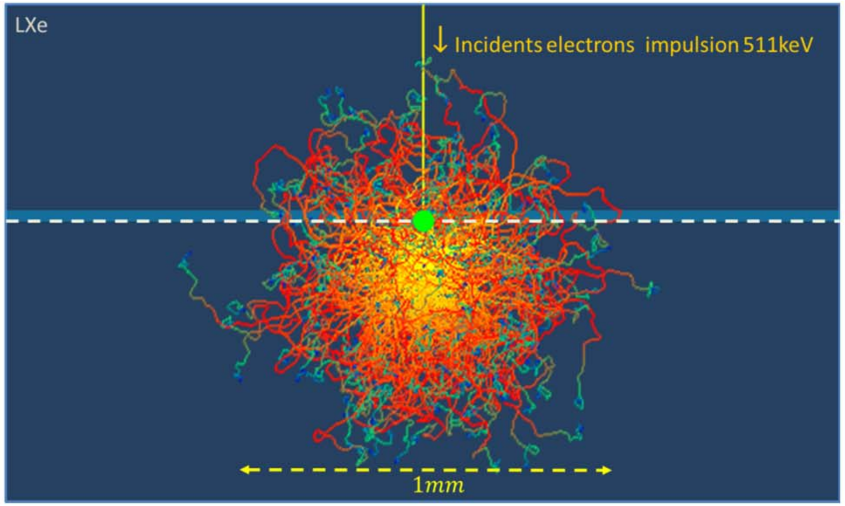
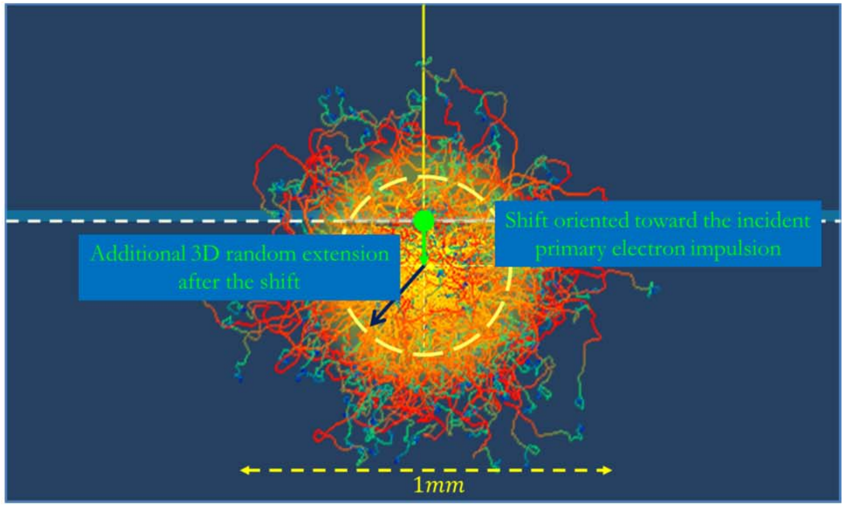
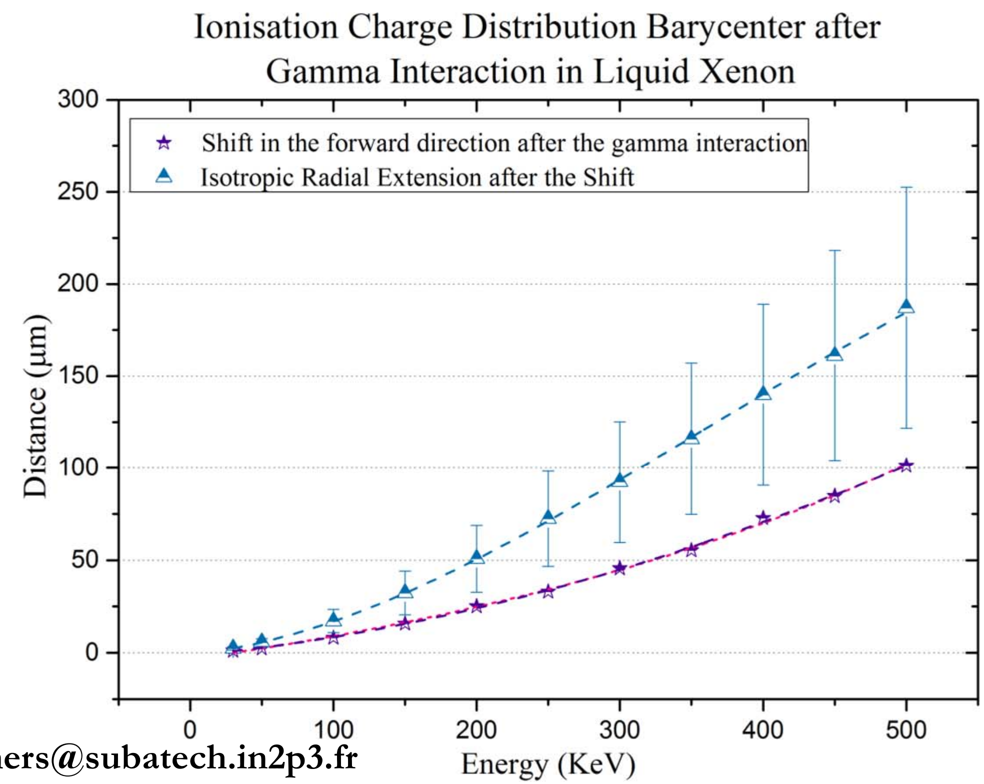
# Electron recoils and ionization cluster in LXe

CASINO : monte CArlo SImulation of electroN trajectory in sOlids (no X-rays)




Parametrization with recombination at 2 kV/cm




Without tracking the primary electron trajectory :
Intrinsic resolution at 100 µm

**LXe TPC for 100 µm spatial resolution on gamma interaction vertices**

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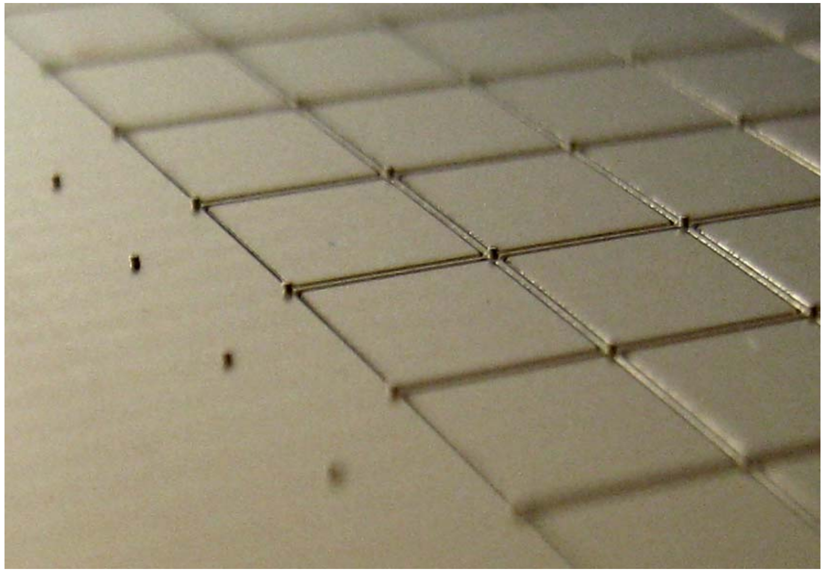
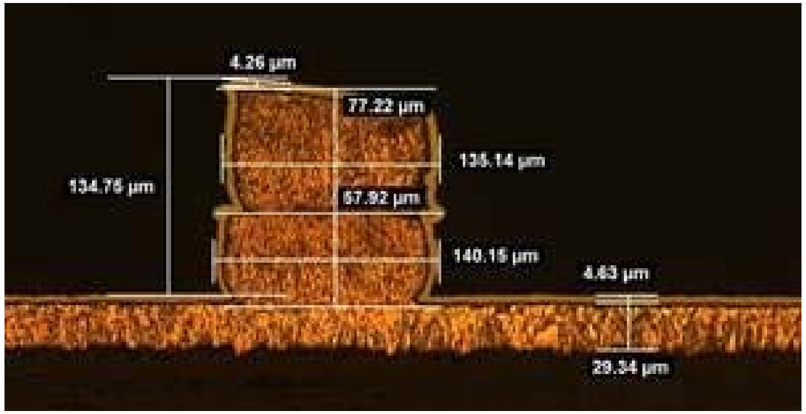
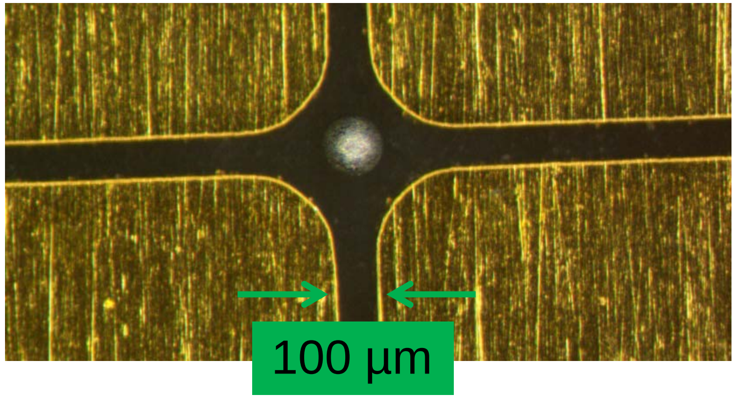
# MIMELI
# (MIcro-MEsh for dense Liquid Ionization Chamber)



Chemically Etched
Very nice but expensive

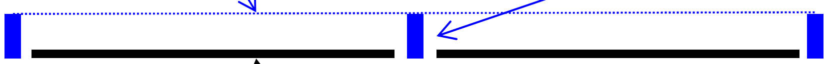



Ball Grid Array welding
Under development
Low cost




µMesh (copper, d ~ 10 µm, 500 Line Per Inch-LPI)

Conductive pillar (g ~ 130 µm)



Pixel p = 3.1 mm, 100 µm isolating

Negligible induction on neighbors pixels (g/p < 5%)
Excellent Frisch grid efficiency (500 LPI µMesh)
Stable on long term (more than 1 year accumulated test)
Scalable on large surface …

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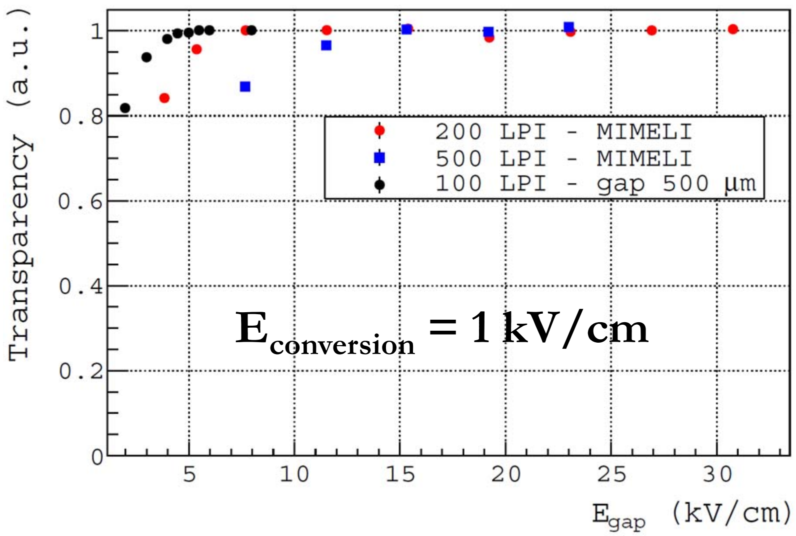
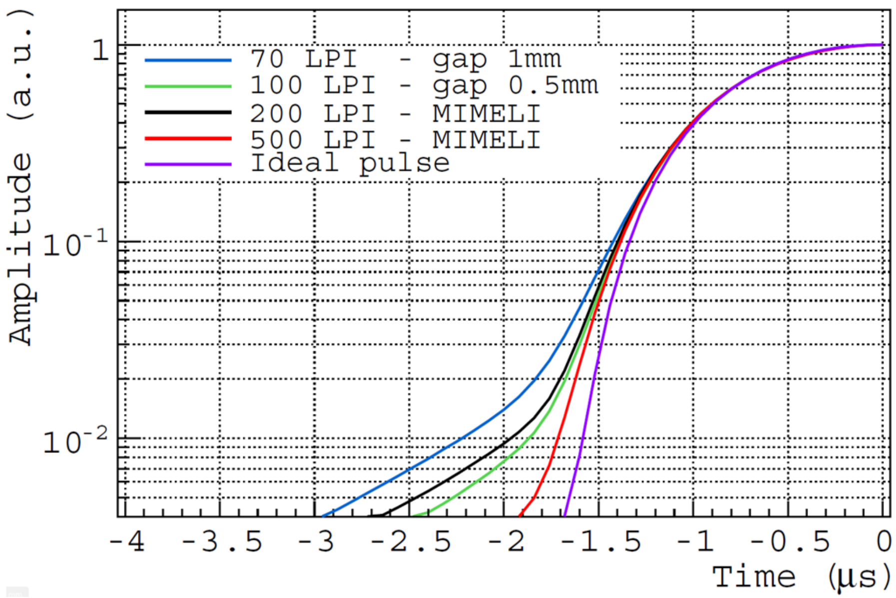
# MIMELI performances




Electron collection > 99%

Negligible current leak
Frisch grid efficiency > 99%

**MIMELI in Liquid Xenon TPC for ultra precise ionization current measurement**

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# MIMELI performances for recoil electrons 3D positions

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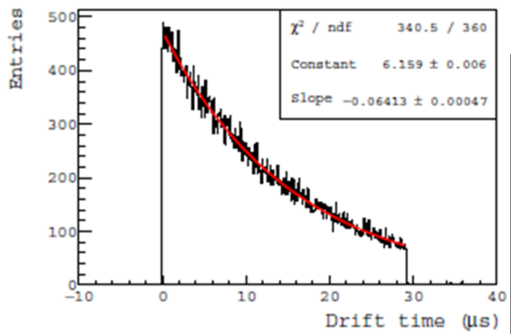
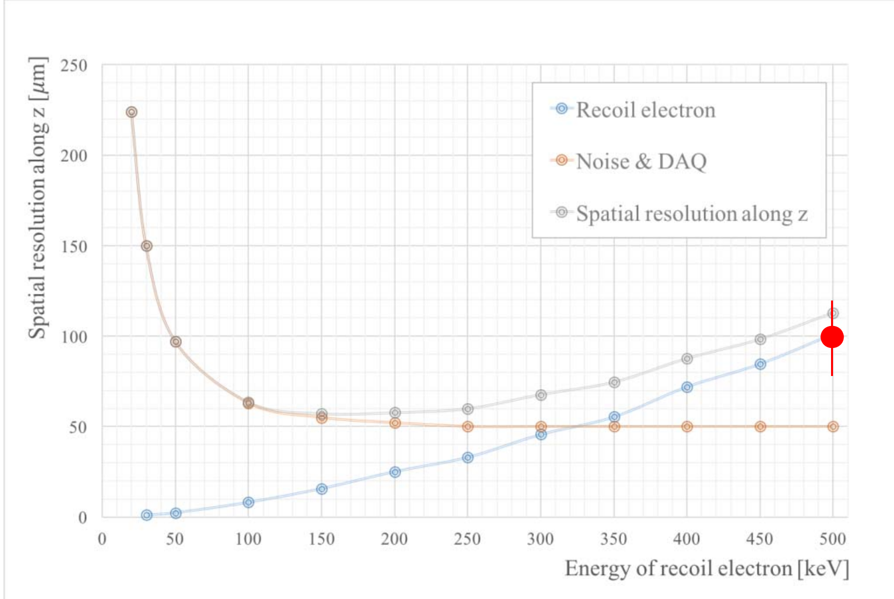
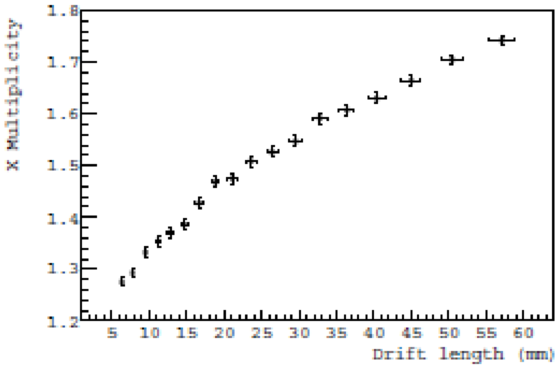
Yajing Xing PhD thesis, work in progress



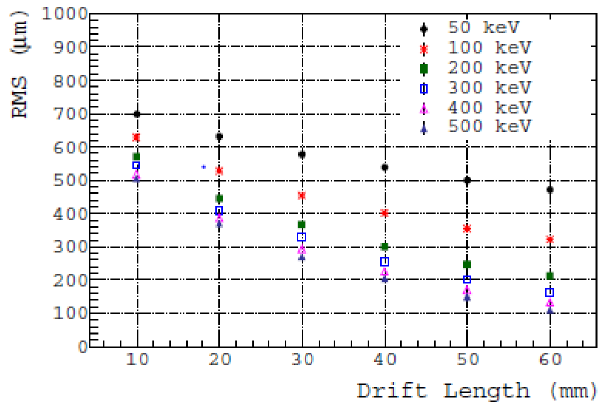

µMesh and cathode edges to measure the z resolution
100 µm measured at 511 keV




Lucia Gallego-Manzano PhD thesis, https://tel.archives-ouvertes.fr/tel-01479948




Transversal diffusion helps to measure the (x,y) positions
100 µm at 500 keV for more than 6 cm of drift with barycenter

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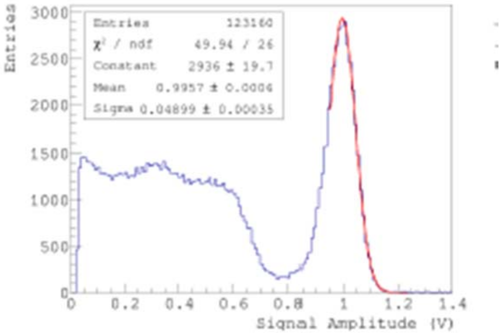
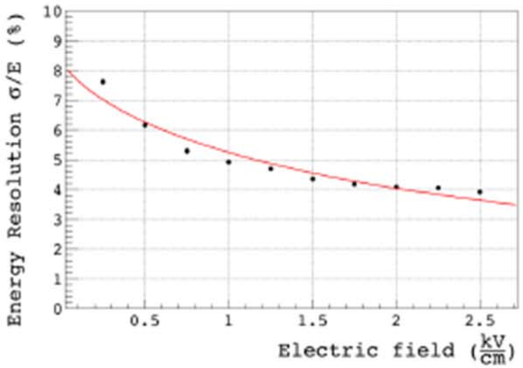
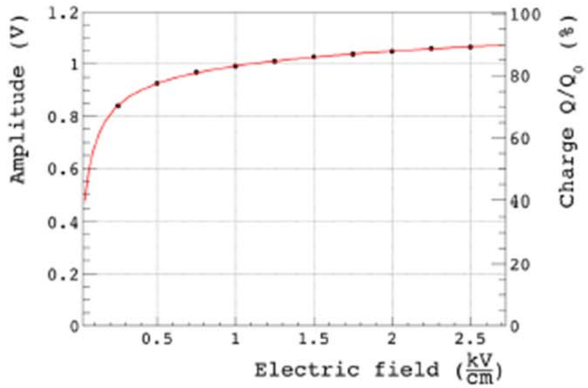
# MIMELI performances for recoil electrons energy

With 511 keV γ calibration line

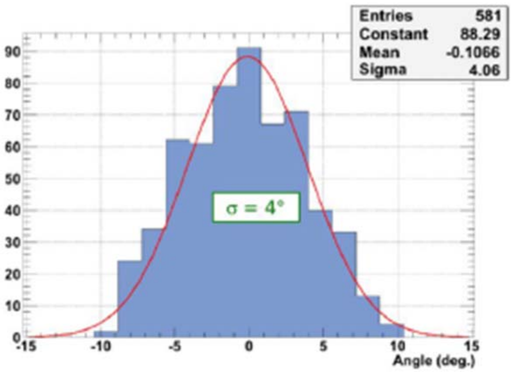


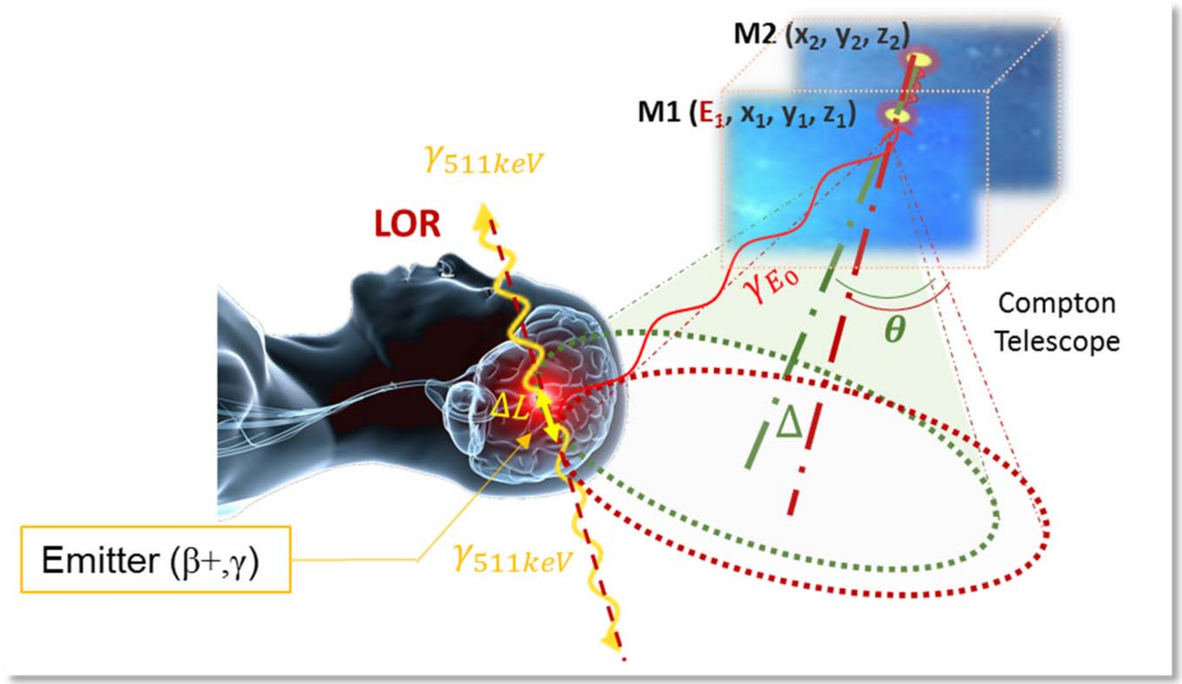




# MIMELI performances for angular resolution

With $^{22}$Na 3rd gamma @ 0,75 kV/cm




**2° targeted at 3 kV/cm**
**work in progress**

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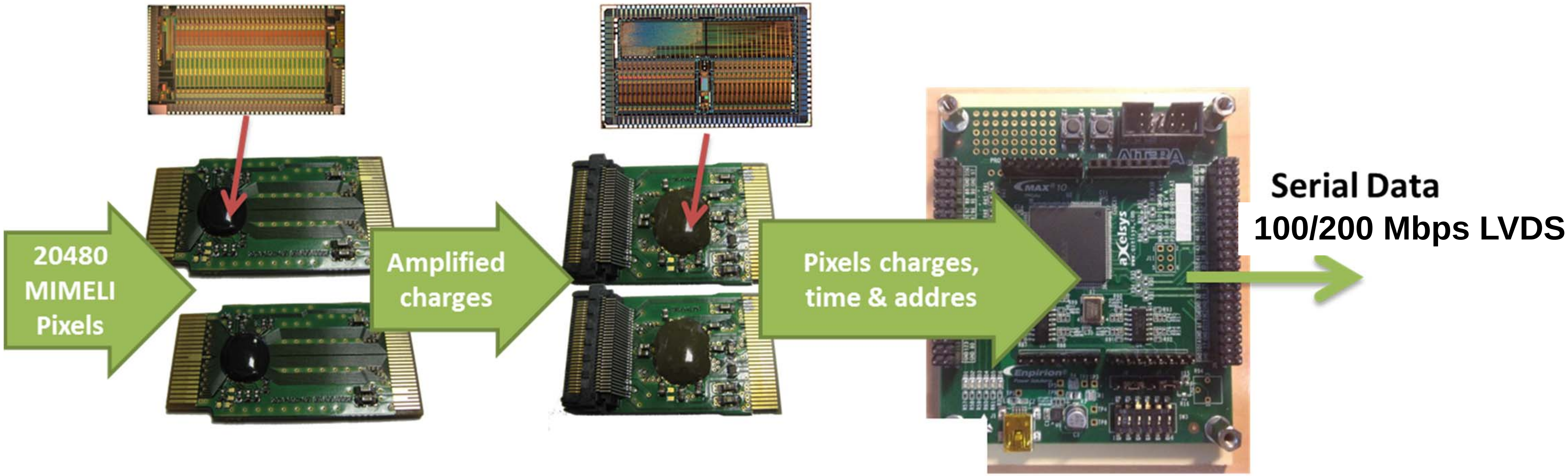
# XEMIS2, electronics

**640 x IDEF-XHD_Lxe**
IRFU – SUBATECH

**640 x XTRACT**
MICHRAU - SUBATECH

**80 x PU**
SUBATECH




**Charge amp**
**Noise = 80 e- ENC**
**Peaking Time 1.39µs**
**Dynamics 80 000e$^{-}$**

**Trigger for each pixel :**
- **Charge**
- **Time**
- **Address**

**Digitalisation:**
**Charge & Time** (ADC 12bits/5MHz)
**~ 64 bits / hitted pixel**

**Rate : up to 4x10$^{3}$ charges/pixel/s**

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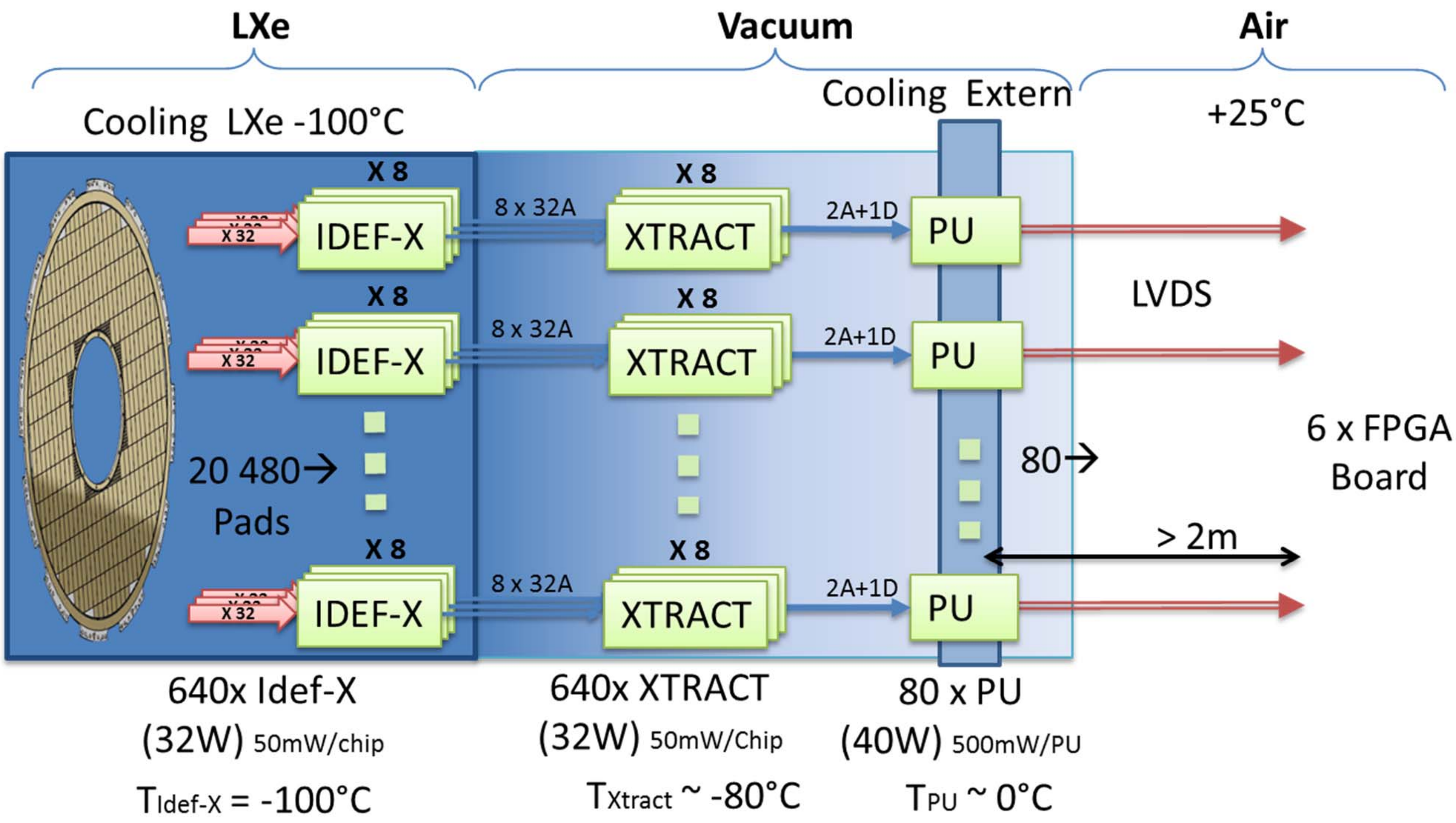
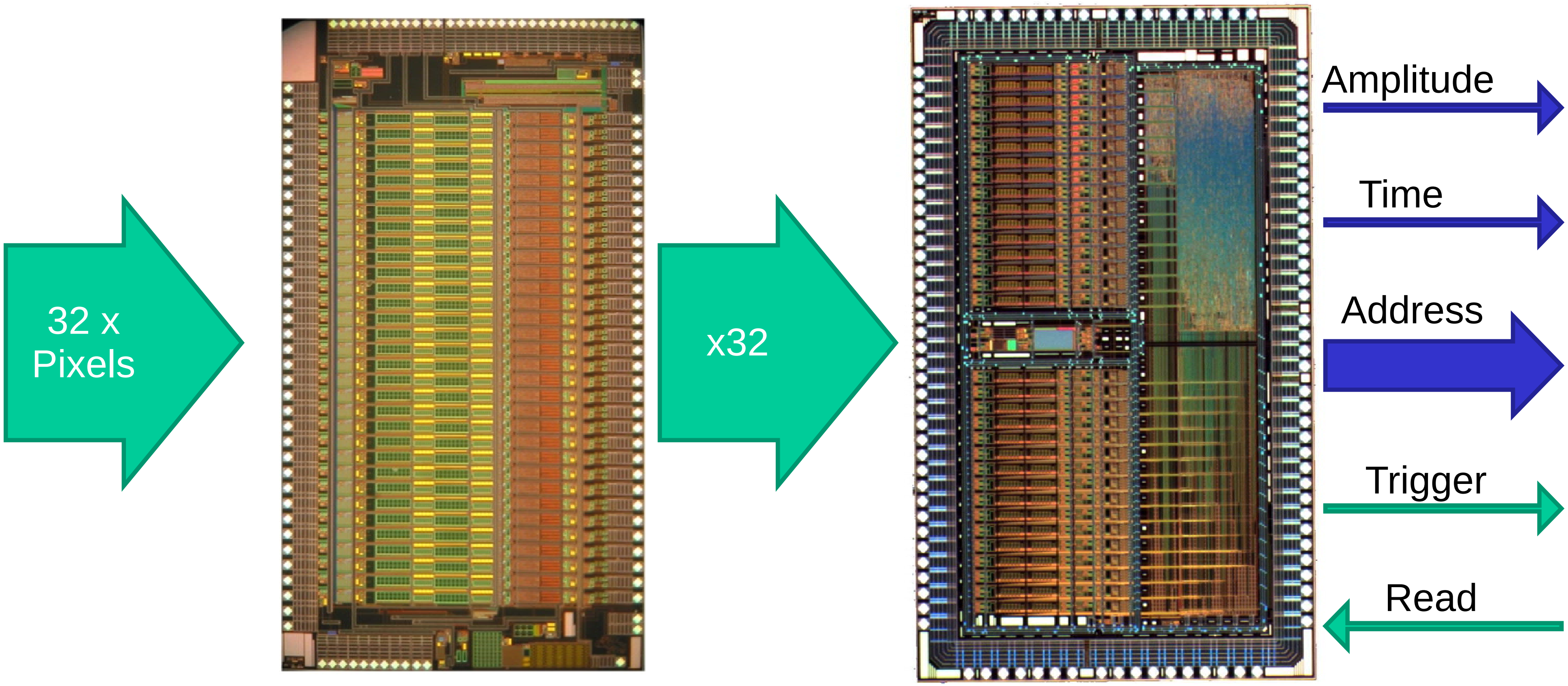
# XEMIS 2, DAQ and Feedthroughs



# XEMIS2 contains specifics µ-electronics

**IDEF-XHD_LXe**
**D**etector **F**ront-end

**XTRACT**
**X**EMIS **T**PC **R**eadout for **A**cquisition of **C**harge and **T**ime




IRFU - SUBATECH

MICHRAU - SUBATECH

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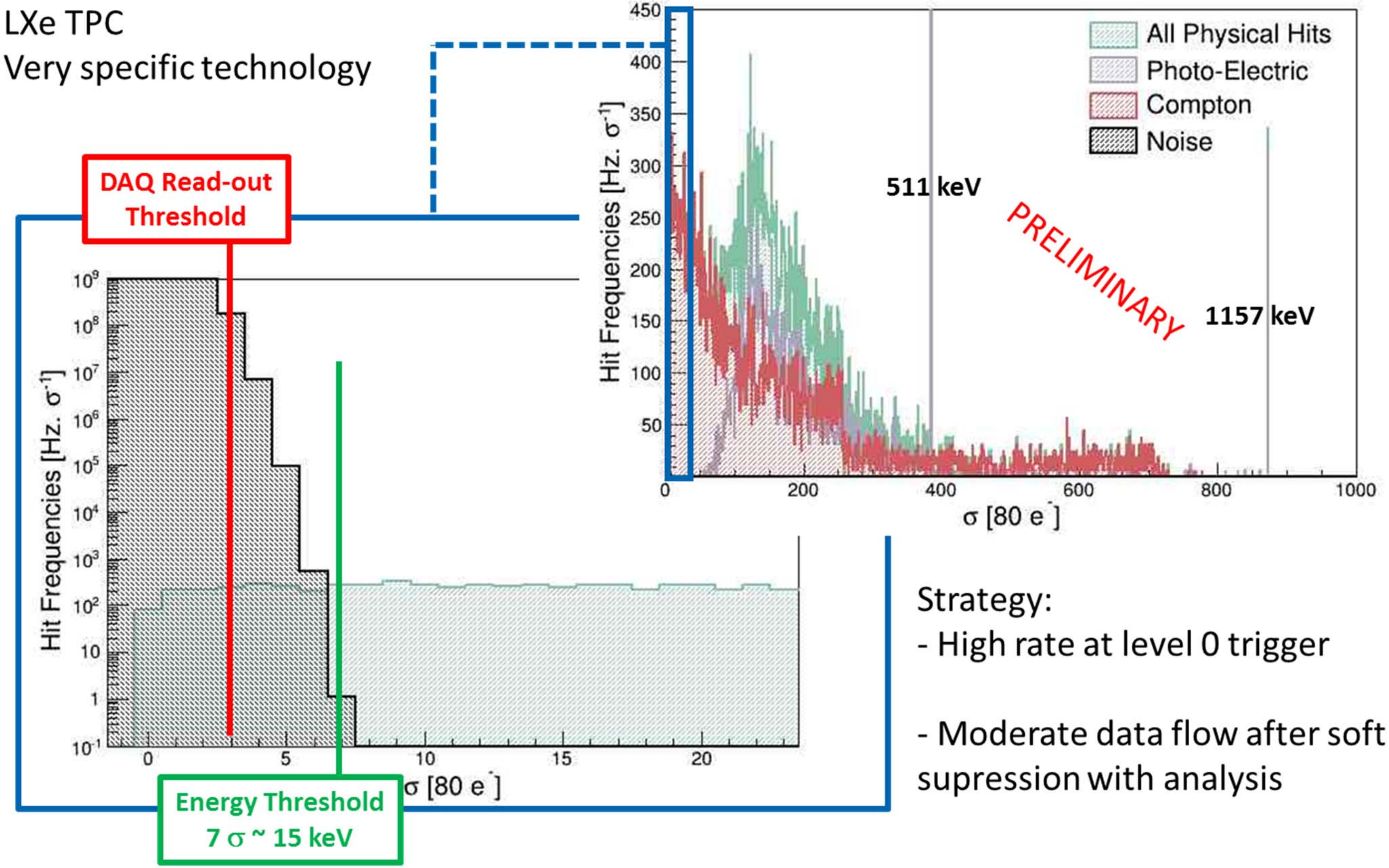
# XEMIS2 : Data flow at 20 kBq

LXe TPC
Very specific technology




Strategy:
- High rate at level 0 trigger

- Moderate data flow after soft zero supression with analysis

**Goal : record small charge on adjacent pixels above 3σ**

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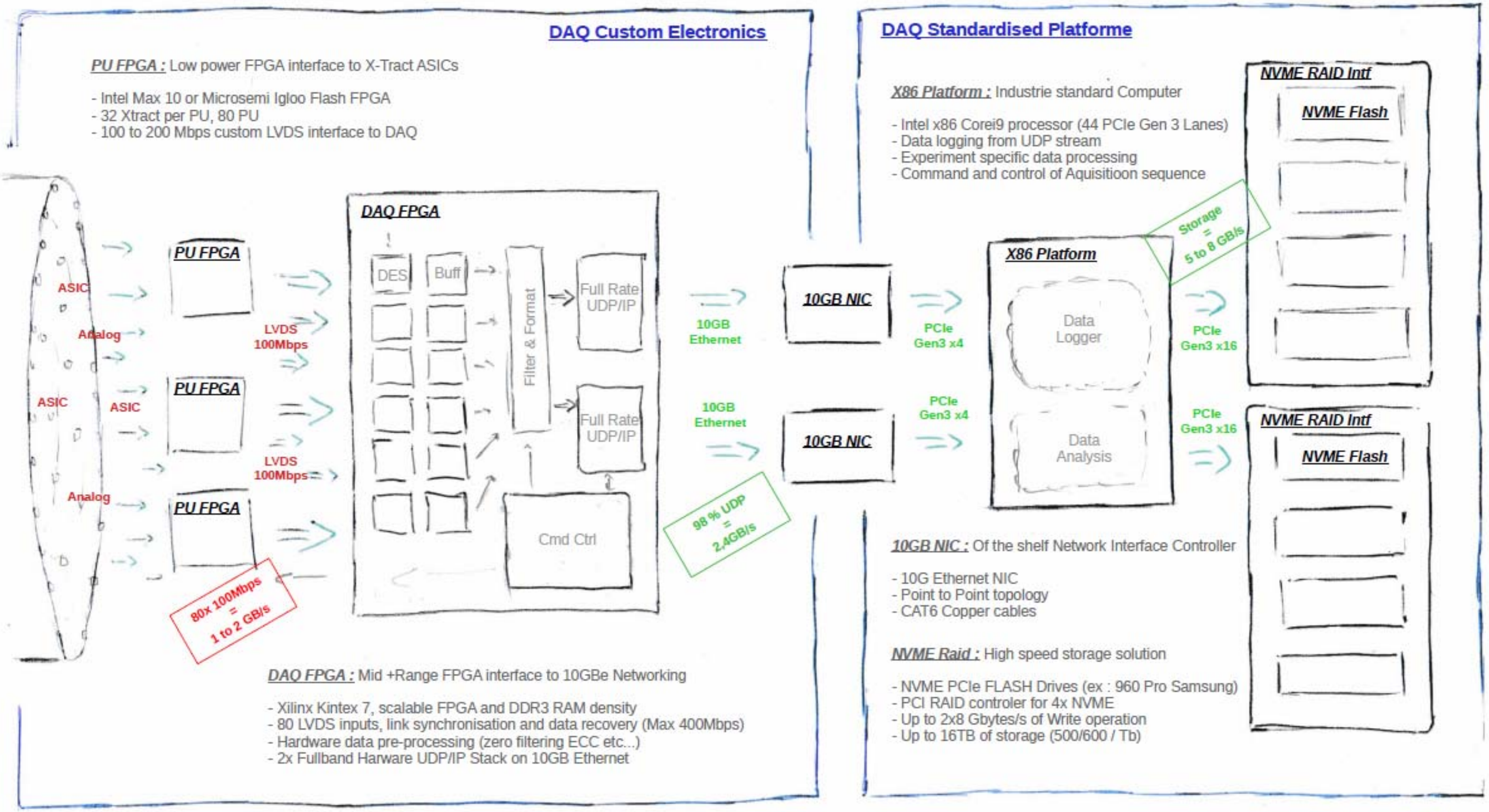
# XEMIS2 : Last DAQ stage for data storage and on-line analysis




- up to 2 TB Storage in 20 minutes with continuous real time files for every 80 ms
- low cost expected
- online soft additional zero suppression under development (from 3 to 7σ)
- online line-cone algorithm crossing under development
- online tracking under development

**First complete DAQ system expected for September, online imaging expected for 2019**

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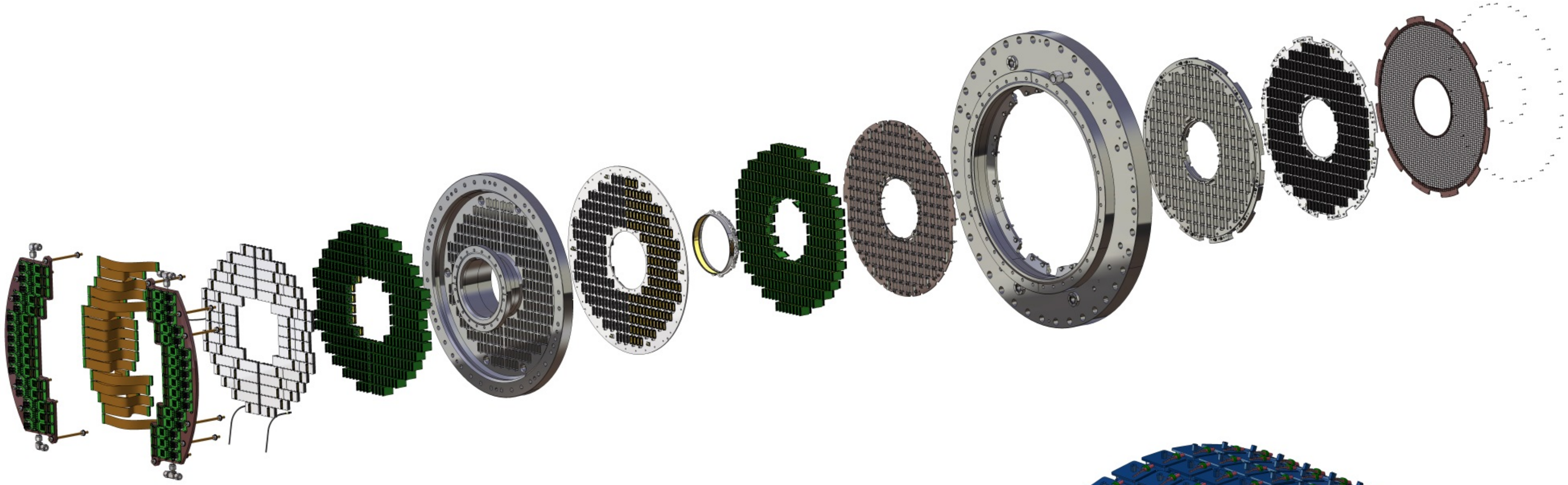
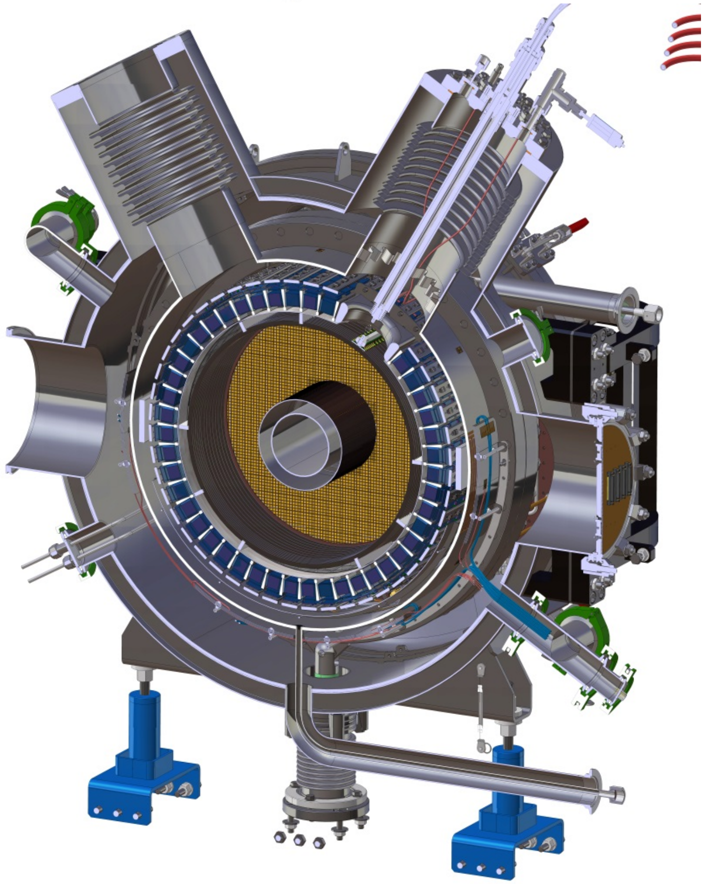
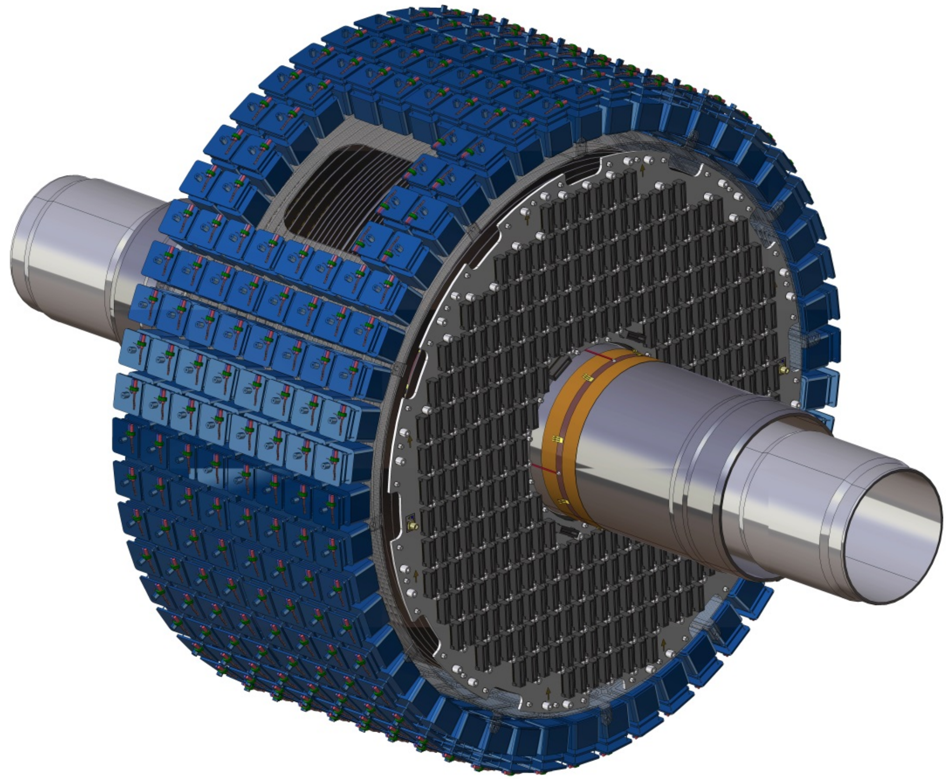
# XEMIS2 Assembling and construction

pôle imagerie défi 10 ps







Inner cryostat instrumented for summer 2018

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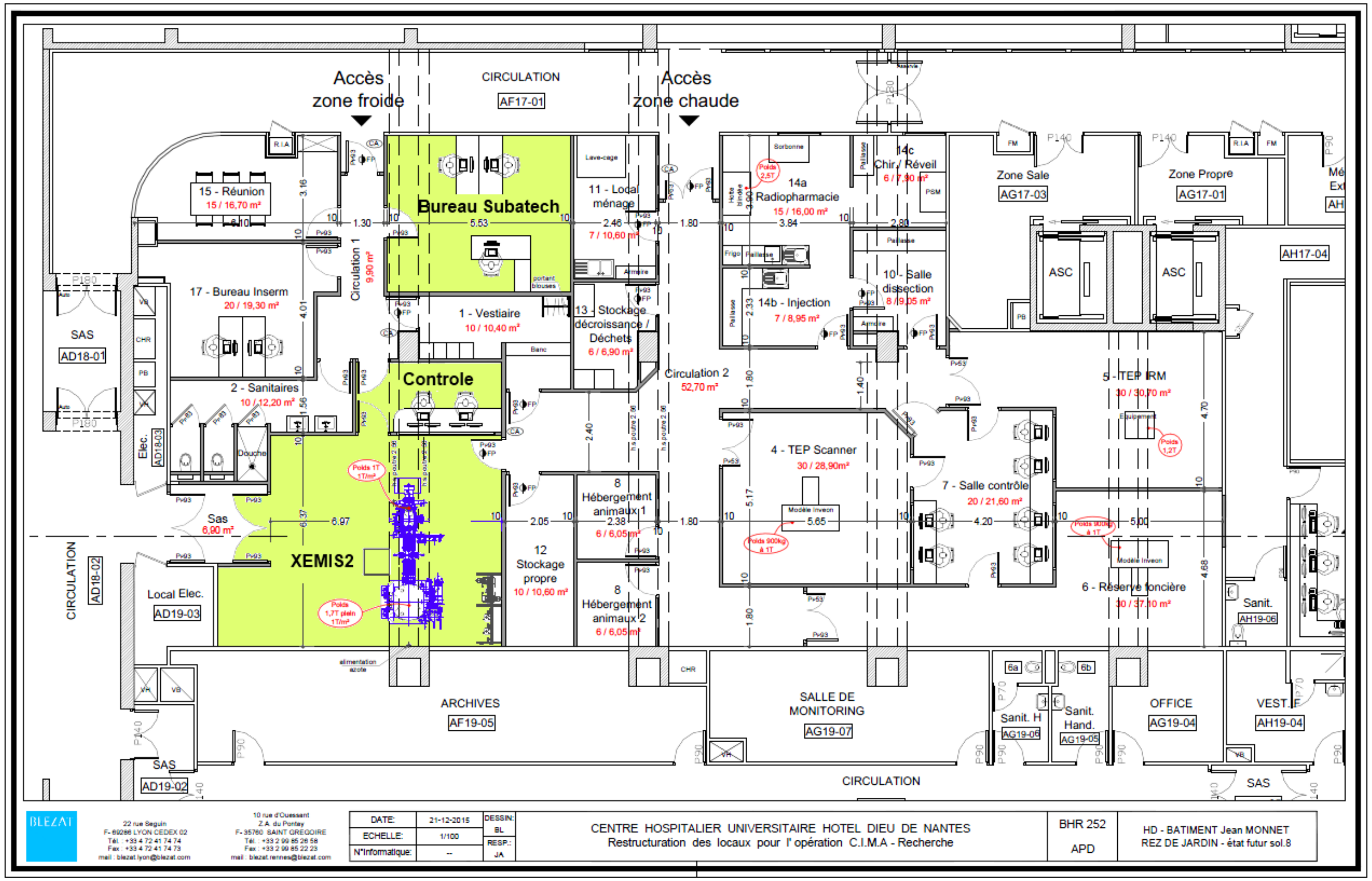
pôle imagerie défi 10 ps

# XEMIS2 Installation at the Nantes hospital

Thanks to a scientific collaboration with :

Inserm

CENTRE HOSPITALIER UNIVERSITAIRE DE NANTES




~ 87 m$^2$ for the camera and control rooms

Installation : Official date 30$^{th}$ June 2018

One year of work before commissioning at Nantes CHU

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# Conclusions

- 3γ imaging is a new medical modality, promising thanks to LXe technology
- We met very nice challenges with the camera design and with its imaging capacity
- Construction of XEMIS2 is well advanced, the potential of this new generation of Compton camera with LXe for medical imaging is reaching the level of the real demonstration
- Expected image qualities are very promising:
  - very low injected activity
  - good spatial resolution all over the FOV
  - reduced acquisition time on a large FOV

LXe technology is scalable: design of large whole body camera can be investigated
We plan to do it from 2020 for Nuclear Medicine

Prompt Gammas for in beam hadron therapy monitoring is reputed to be very challenging
It could also benefit from this new kind of camera

# Hadron/Proton therapy : Clinical treatment of Radiotherapy Hospital Dpt

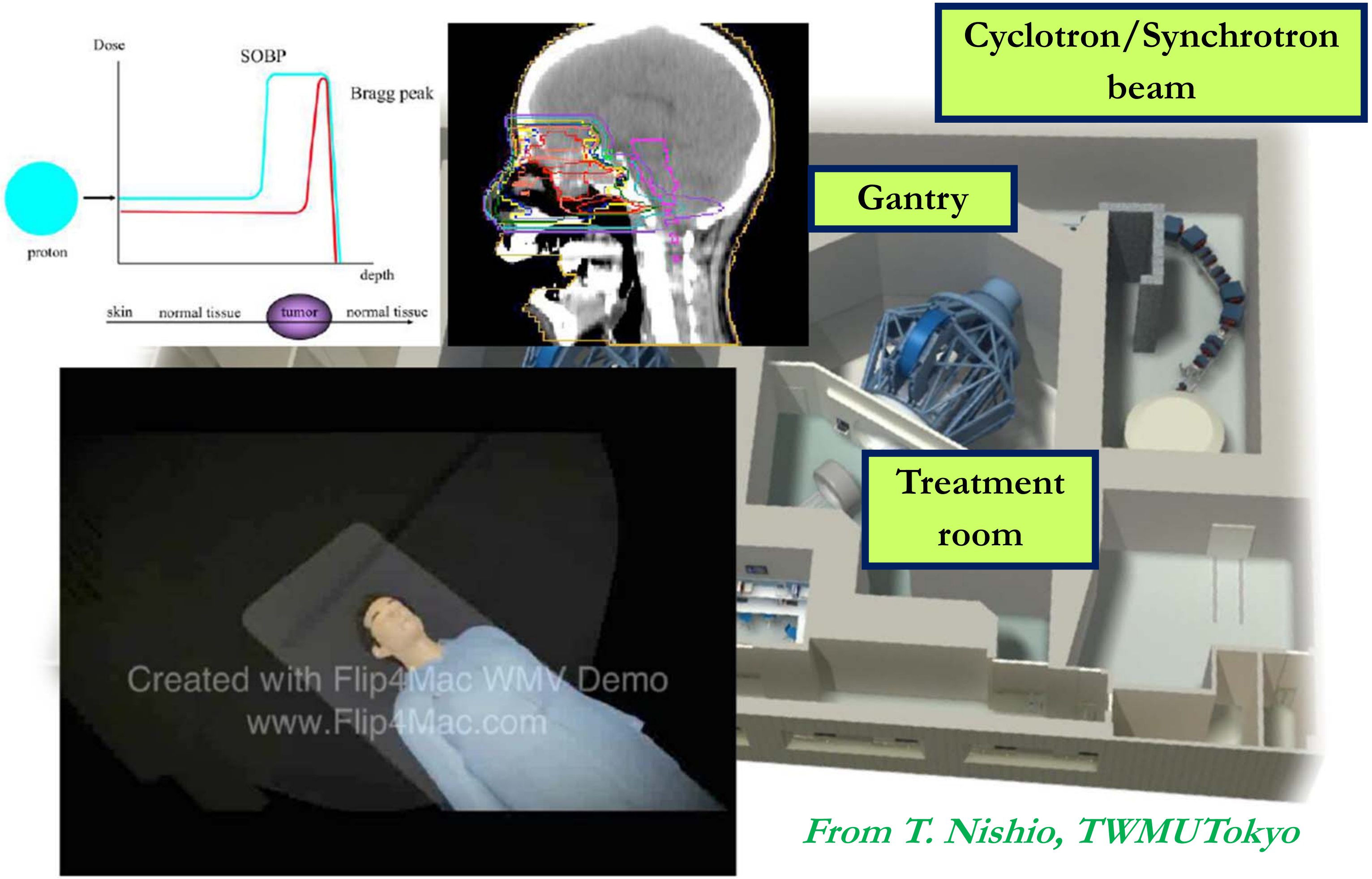
## Proton therapy

**Heavy Infrastructure:**

- Beam
- Gantry

➢ More than 20 years live time

➢ "State Investment" for generations




*From T. Nishio, TWMUTokyo*

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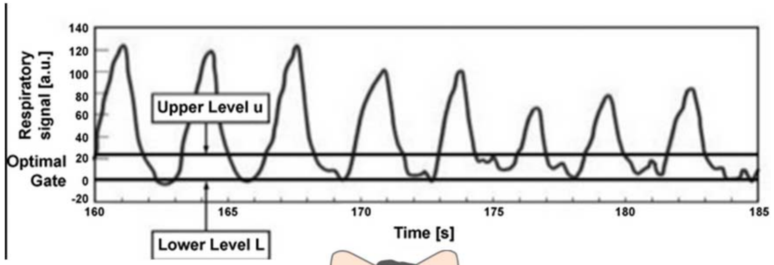
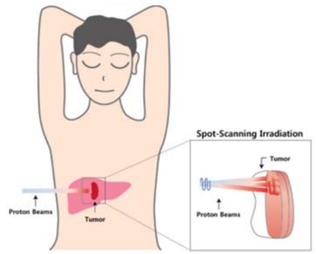
# Present treatment planning



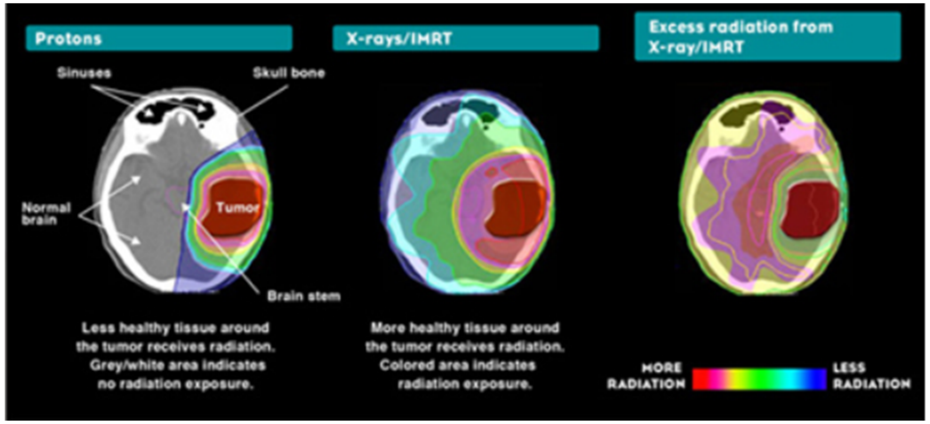

## Before each treatment

1/ CT and MR Images (4D planning)
2/ Dose simulation
3/ Dose optimization with ballistics selection
- Patient position
- Beam energy and position (gantry for treatment in depth)
- Spot scanning and expiration gating

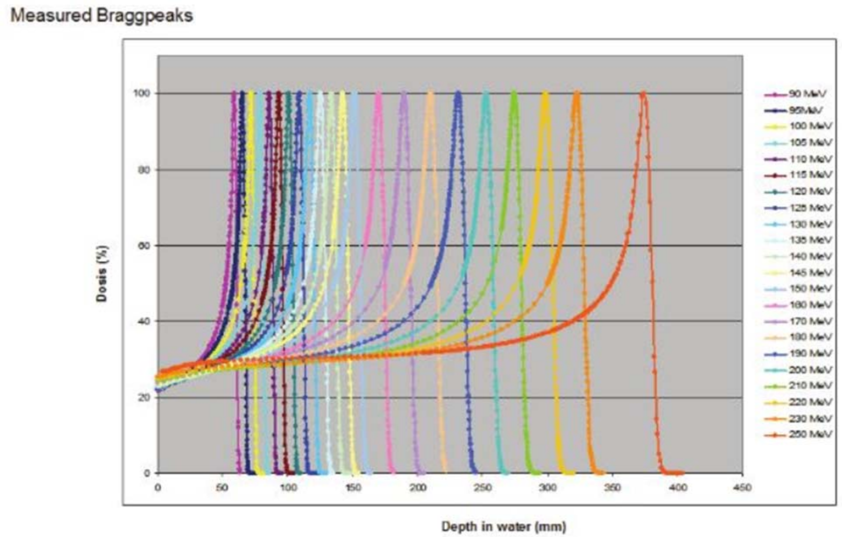



**No online monitoring:**
**Beam and tumors are not observed during treatment**

➢ Gantry for high energy treatment




➢ Less dose with hadron and proton than with γ




Precision in the penetration depth, variable proton energy to guarantee coverage of the tumor (measured at the RPTC)

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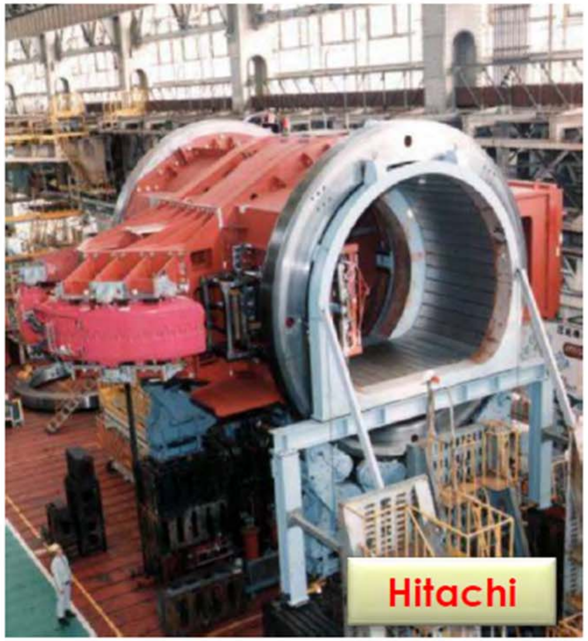
# Rotating Gantry

- **Proton therapy**
  - Gantries are commonly used
  - Commercially available
- **Carbon therapy**
  - Required Bρ is 3 times higher
    - Magnets will be very large and heavy
  - Difficult to
    - Design
    - Construct






*From Y. Ywata, NIRS-HIMAC*

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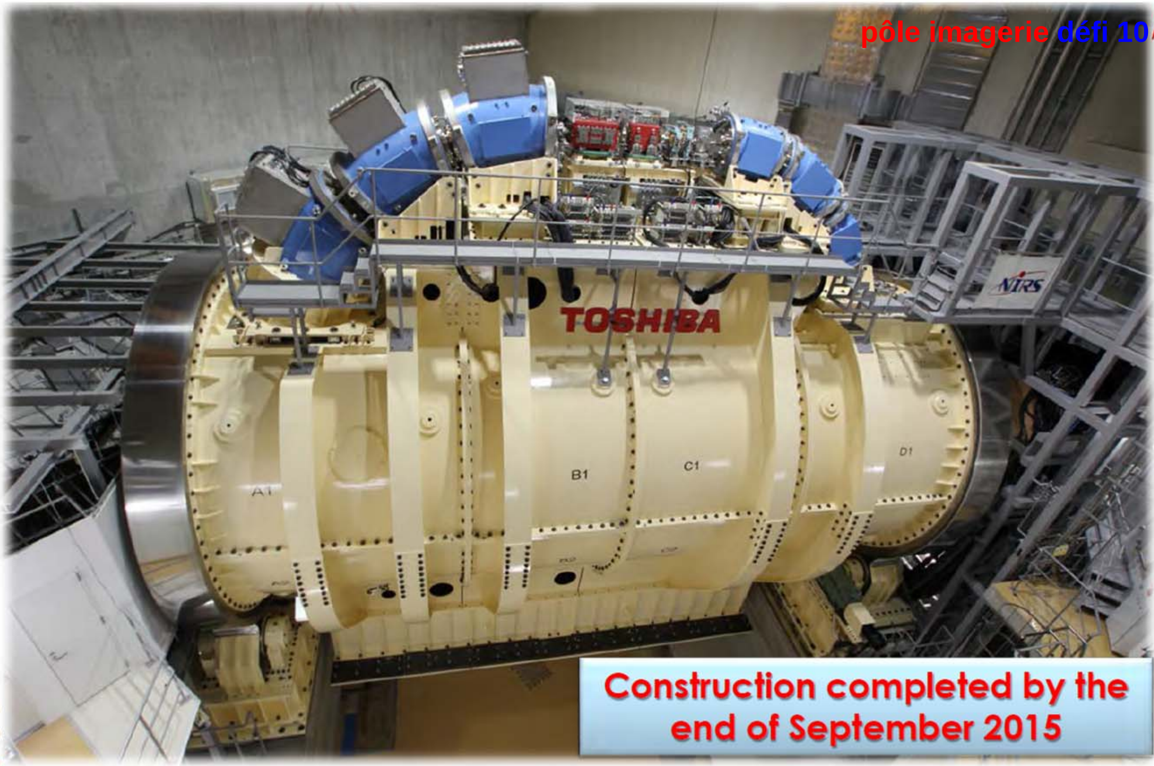
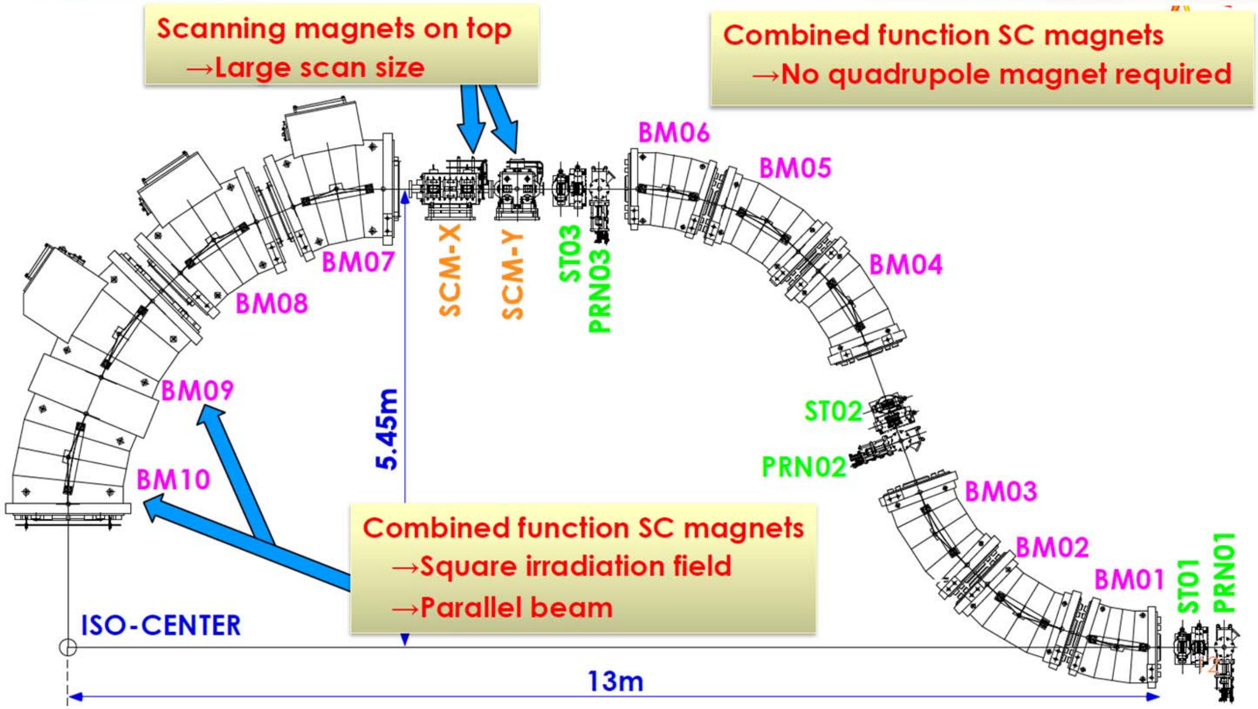
# Super Conductive Gantry for carbon beam

*From Y. Ywata, NIRS-HIMAC*




NIRS HIMAC

## Layout of the




Weight: only 300 tons !
Beam energy: 430 MeV/u max
Range in water: 30 cm

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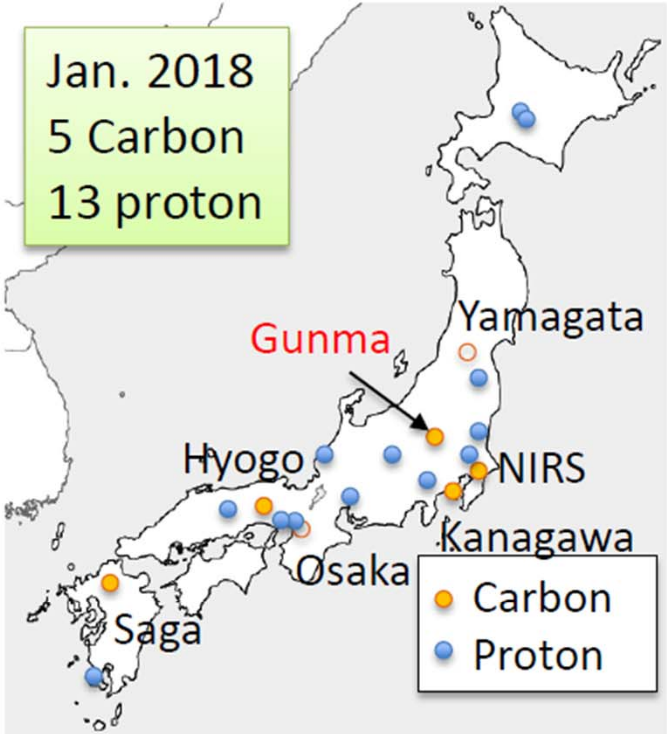
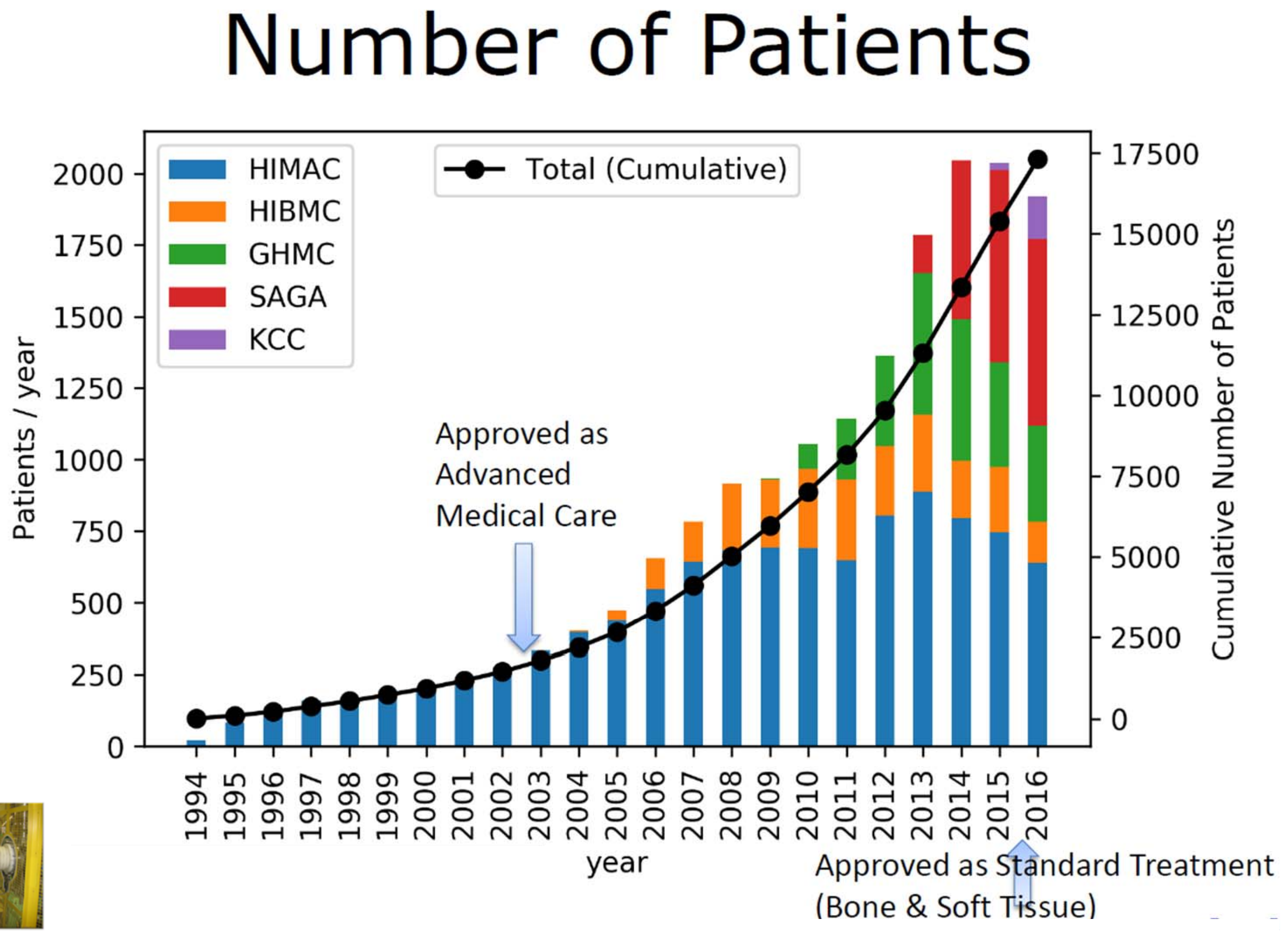
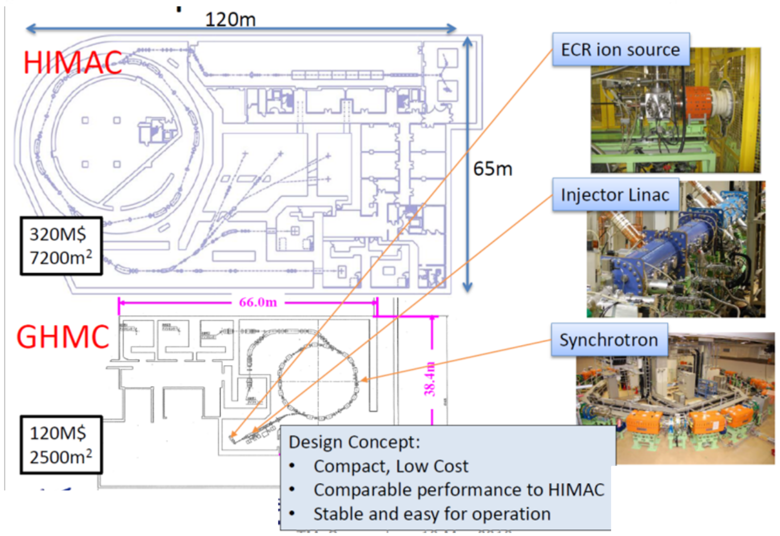
# Hadron therapy in Japan




*From Y. Souda, Gunma University HMIC*




➢ **Japan is the incontestable world pioneer and leader in hadron/proton therapy**

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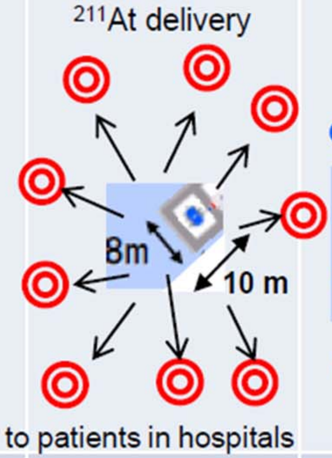
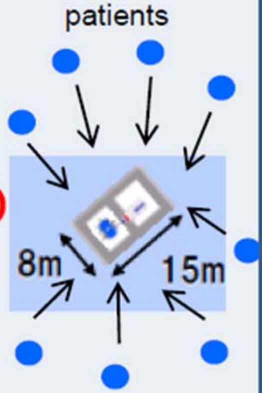
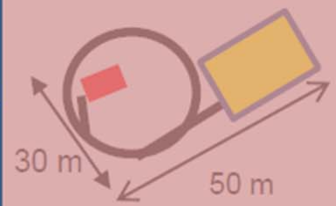
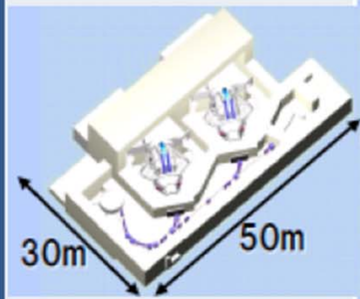
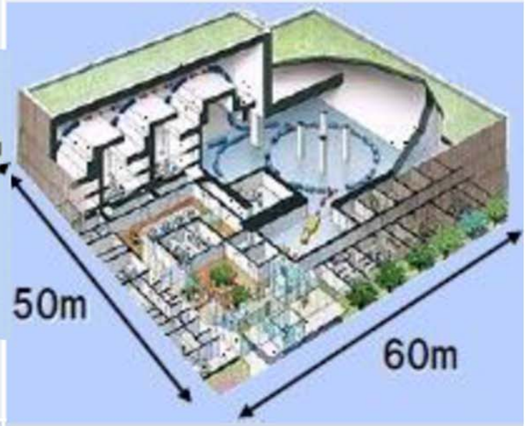
# Accelerator driven cancer therapy

| | Low Cost Therapy | | Hadron Therapy | | |
|---|---|---|---|---|---|
| | $\alpha$-Therapy | BNCT | Next generation (p/He3/C) | Proton | Carbon |
| Space requirement |  |  | no injector<br>no gantry<br> |  |  |
| Energy (MeV) | 30 | 30 | 250/300/200 | 230 | 400 |
| Accelerator | Cyclotron | Cyclotron | Induction synchrotron | Cyclotron/ Synchrotron | Synchrotron |
| Cost (M$) | 7 | 10-15 | 40 - 50 | 60 - 70 | ~ 150 |
| Fee (k$) | 3 ? | 10 ? | 20 ? | ~ 30 | > 30 |
| status | under development | Clinical trial is going on. | under development | running | running |

*From K.Takayama, KEK*

➢ Low cost hadron/proton therapy in the future ?

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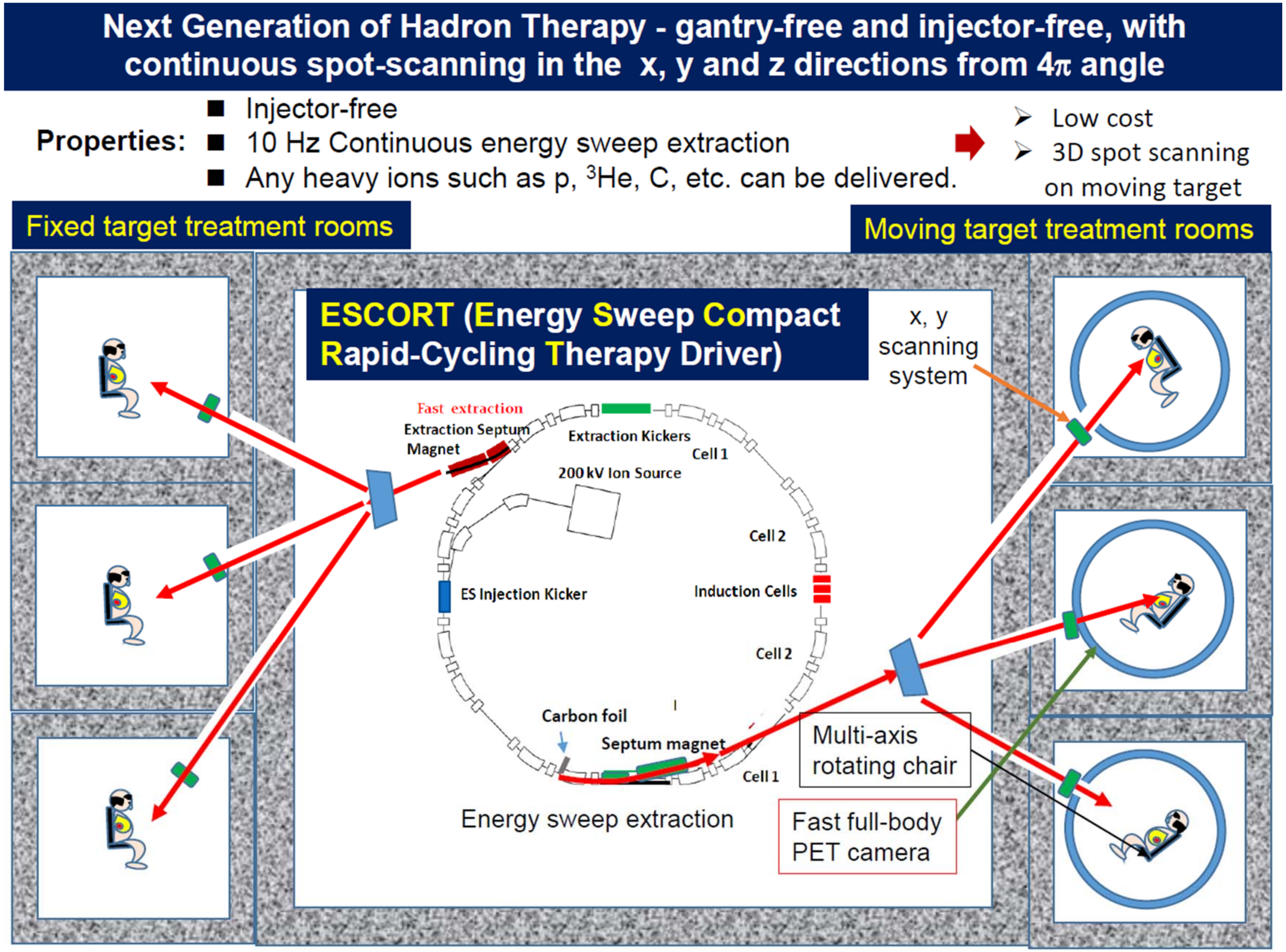
# Alternative low cost hadron/proton therapy center




*From T.Dixit, SAMEER*

- Need to image online beam on tumors
- Need new generation of camera

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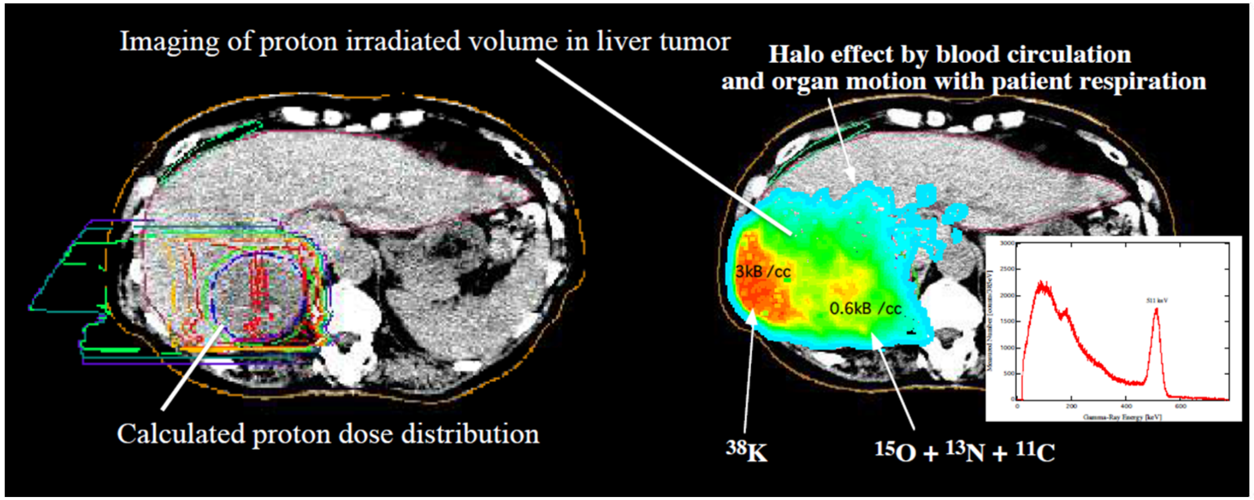
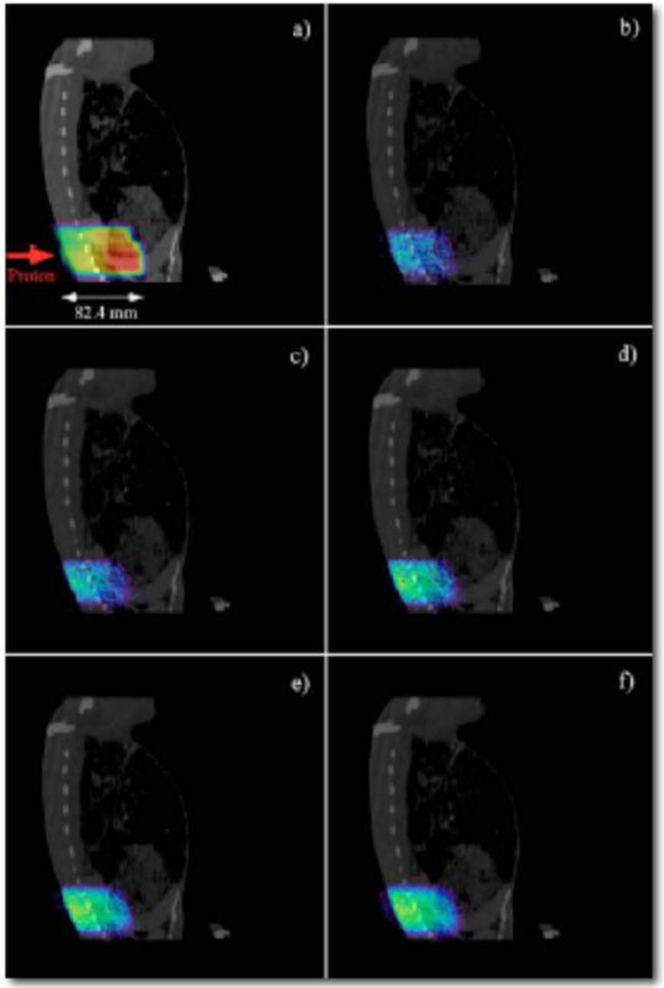
# PET and hadron/proton therapy




*From T. Nishio, TWMUTokyo*




Calculated proton dose distribution (a) and PET image measured at 1 (b), 2 (c), 4 (d), 10 (e), and 30 minutes (f) after proton irradiation in plan 1.

- Off-beam and In-beam PET are facing big issues :
  - $\beta^+$ production by the beam with long half time
  - Beam Bragg Pic not accessible on line

- XEMIS as an alternative thanks to :
  - Tumor localization with 3γ labelling ($^{44}Sc$ not produced by the beam)
  - Online beam monitoring capacity

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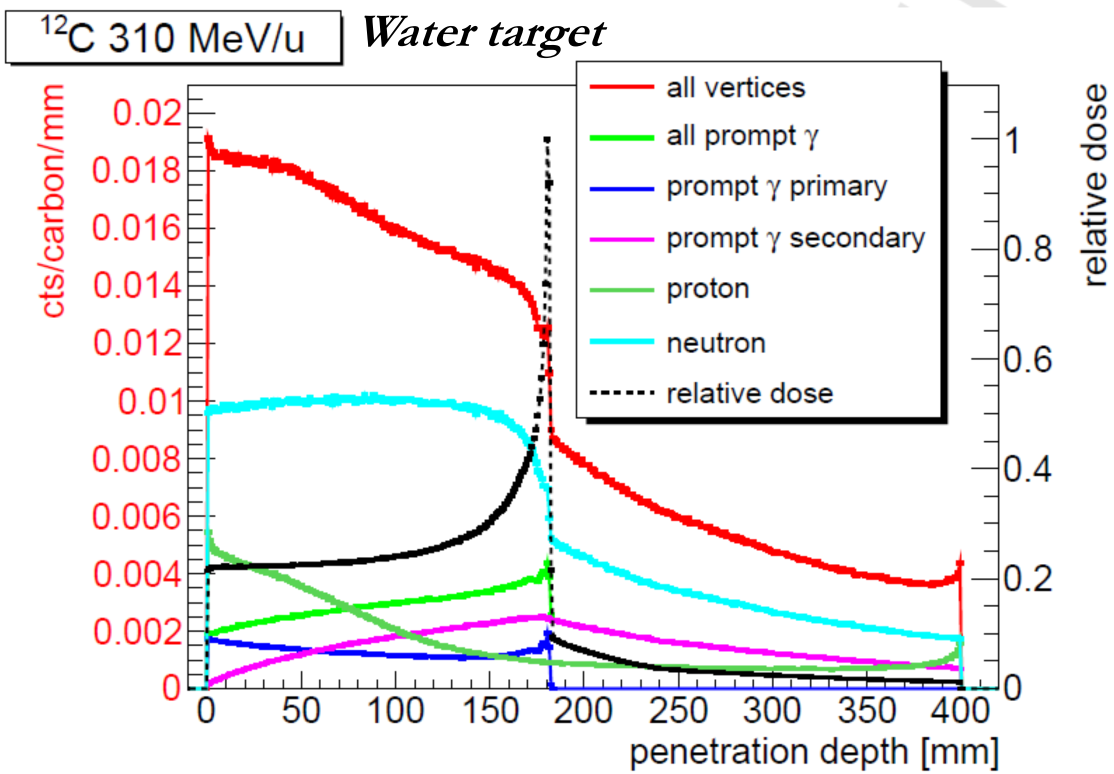
# Prompt Gammas and $^{12}C$ therapy

*From J. Krimmer, D. Dauvergne, J.M. Létang, E.Testa, Prompt-gamma monitoring in hadrontherapy: A review, Nuclear Inst. and Methods in Physics Research, A (2017).*




Prompt Gammas :

- Fallof very closed to the Bragg peak
- Low statistic for primary:
  around $2.10^{-3}$/ion on the last mm
- Secondary PGs: largely distributed
- ~ 0.3 PG/ion
- PGs are mostly isotropic
- PGs are largely distributed in energy until more than 7 MeV
- Neutrons are dominating

Ideal Compton camera :

- largest geometrical acceptance due to the low statistic
- several attenuation lengths for the calorimetry of MeV gamma rays
- precise angular resolution to achieve mm precision along the beam (1D)
- insensitive to neutron (the best), with a very good neutron/gamma rejection power (the minimum)
- synchronized with beam micro bunch structure to separate delayed information from prompt signal
- usable with a 3D rotating bed
- moderate cost

**XEMIS Compton LXe camera is well positioned …**

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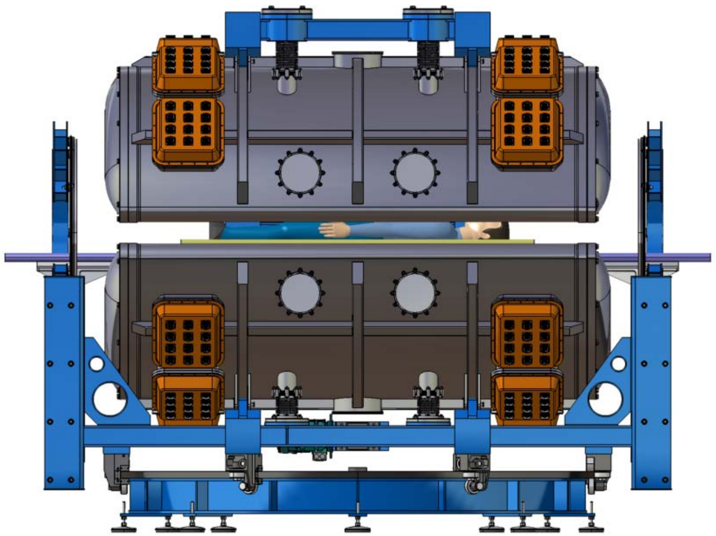
pôle imagerie défi 10 ps

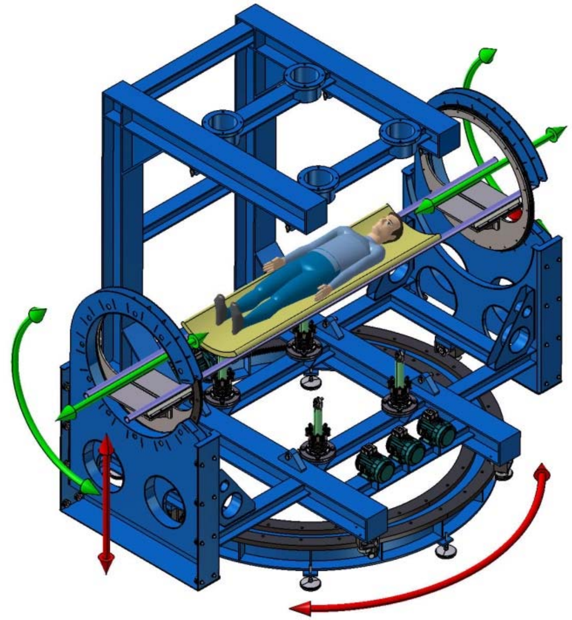
# Geometrical acceptance, what is possible ?

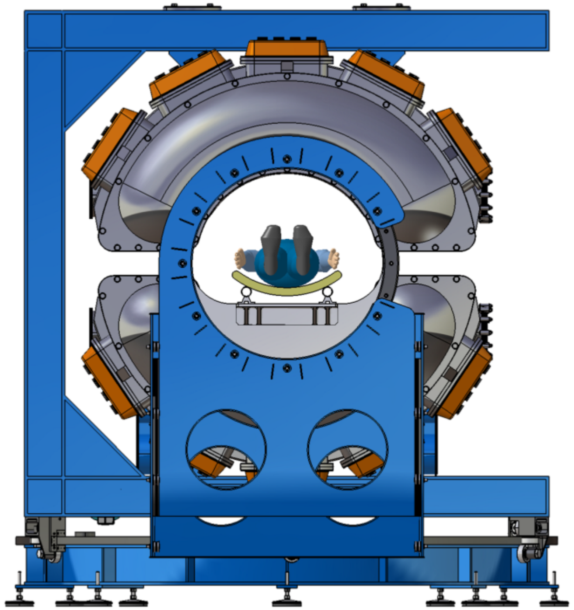


Patient bed could translate horizontally

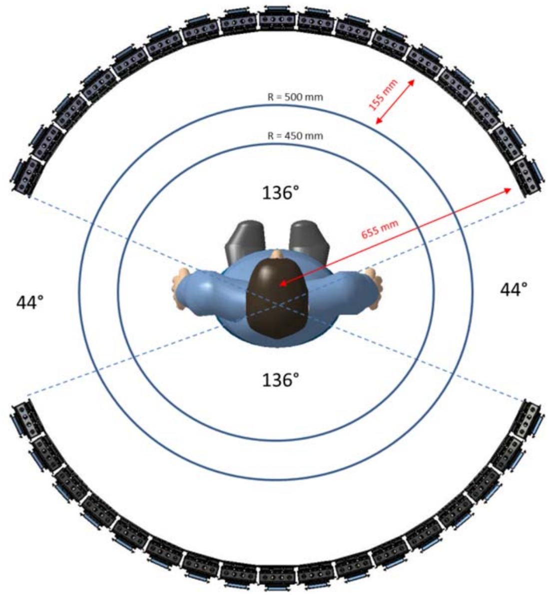
Patient bed could rotate axially

Camera and patient bed could rotate horizontally and translate vertically





Geometrical acceptance
up to ~ 50% feasible
with 2m active length
25% per half-barrel




**R&D required with cryogenics, mechanics and xenon handling**

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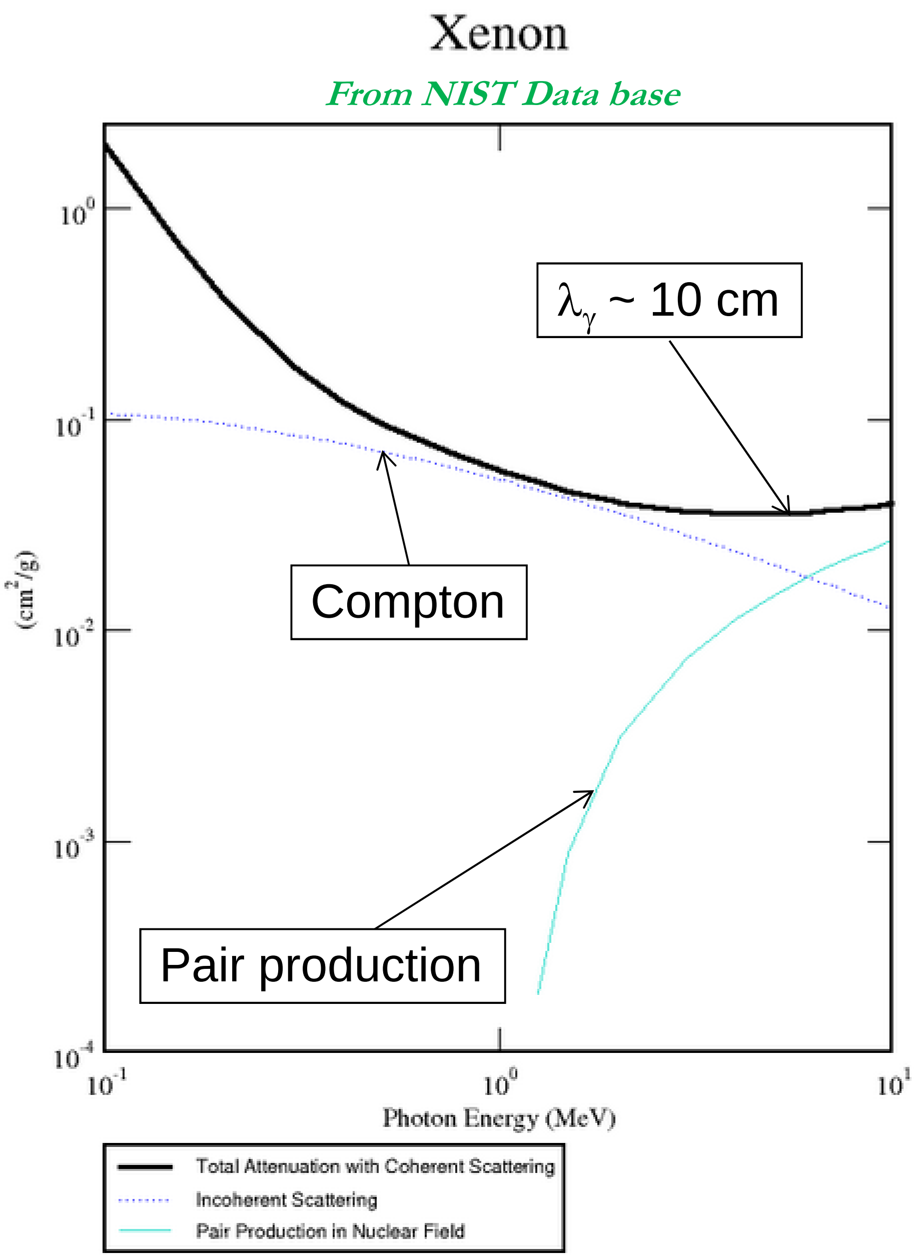
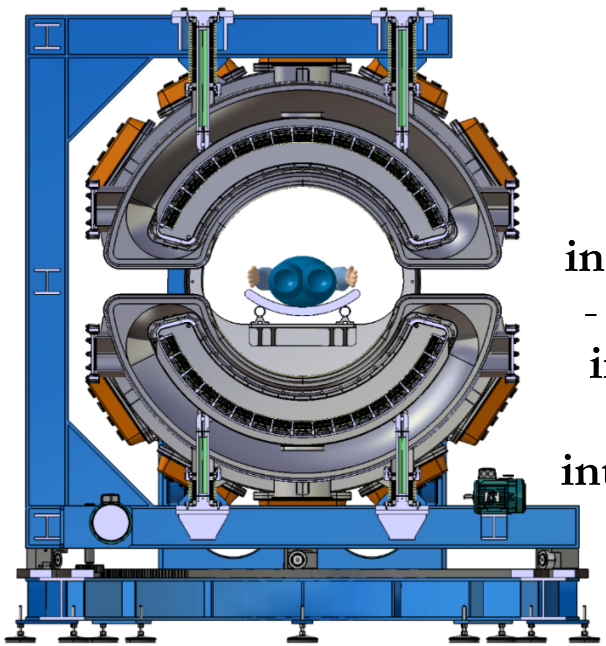
# PGs: MeV γ-rays calorimetry and attenuation




**MeV γ-rays :**
Most difficult region for sensitivity
longest attenuation length
up to 10 cm of LXe @ 4 MeV

**PGs :**
Mainly Compton interactions in LXe, but high energy recoils electrons
Pair production to be considered



Raw estimations :
- up to 25 % of PGs fully calorimetrised
- up to 90 % of PGs interact with Compton first
- less than 30 % of PGs interact with patient first
- less than 5% of PGs interact with camera windows

~ 15% of PGs detectable

**R&D required with expected PGs distribution and Geant4**
**R&D for high energy electrons recoils detection**

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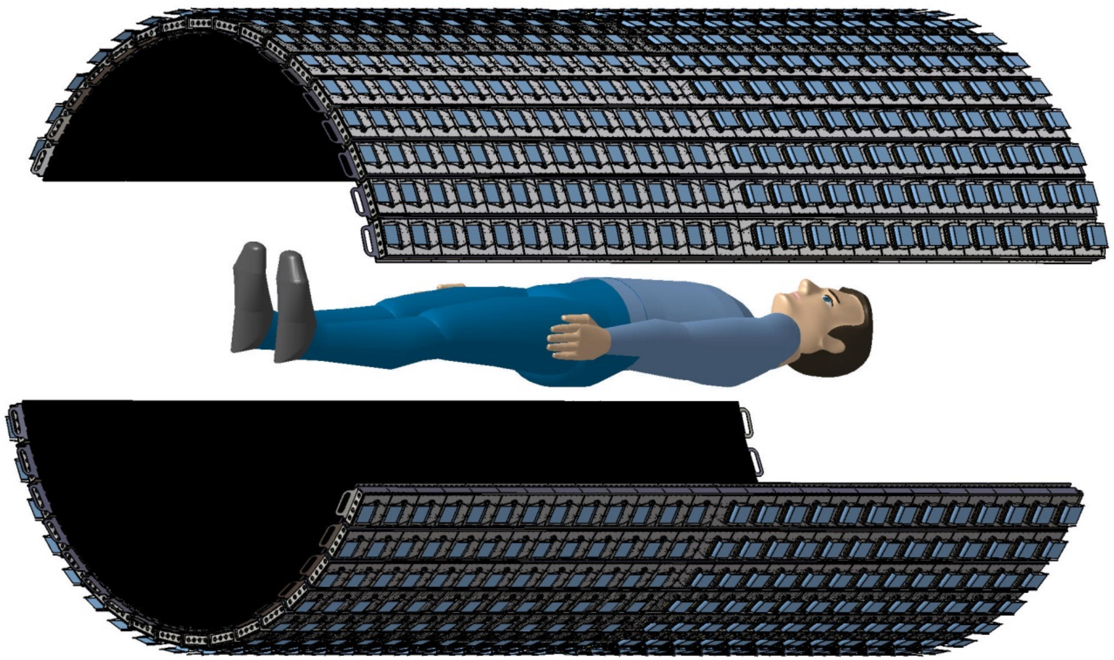
pôle imagerie défi 10 ps

# Radial drift of the electrons for XEMIS-HT scale

For whole body scale:
in radial direction, $E_{drift}$ can be quite uniform
thanks to the higher radius

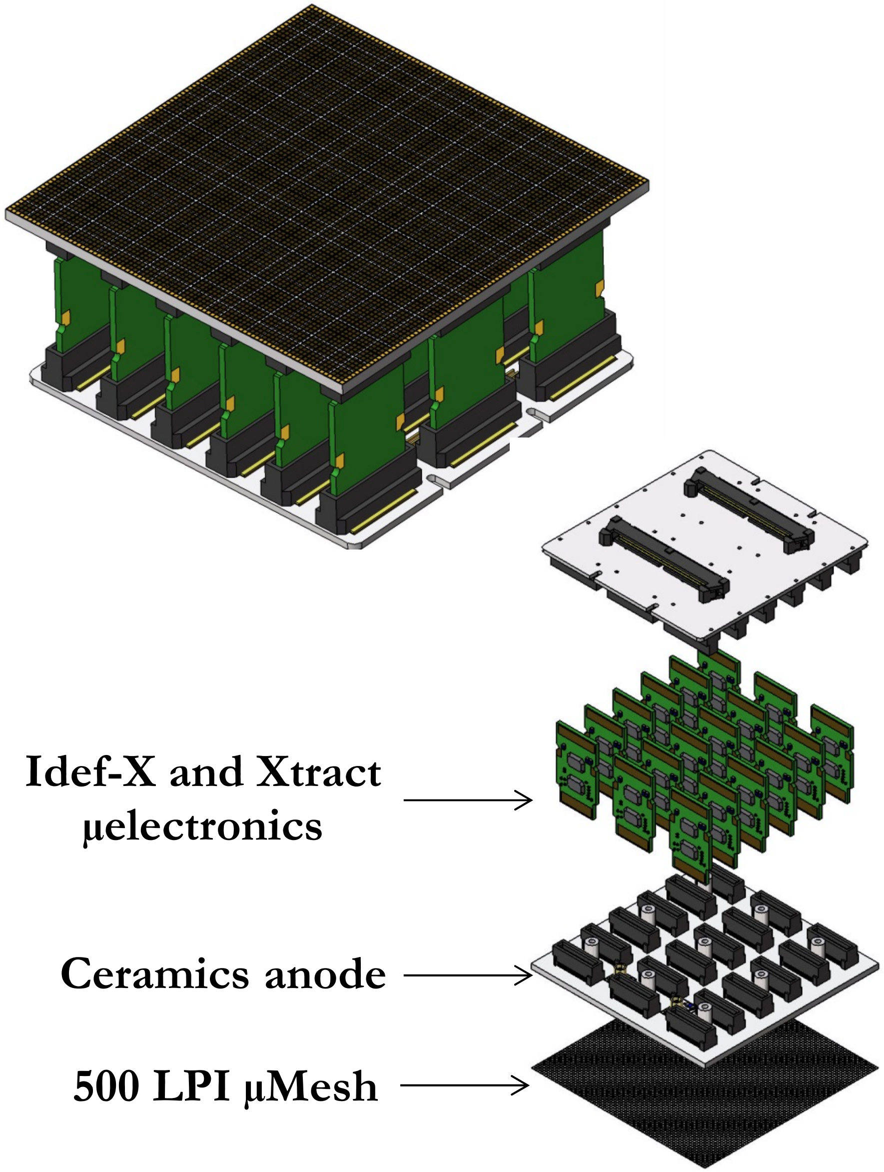
2-3 kV/cm $E_{drift}$
achievable on the whole active volume



~ 250 000 pixels for each half barrel
~ 900 MIMELI units for the camera

XEMIS2 resolution scalable to XEMIS3
2° of angular resolution for PGs

1 MIMELI unit : 9 x 64 pixels
(pitch 3.1 mm)




R&D required with mechanics and electronics

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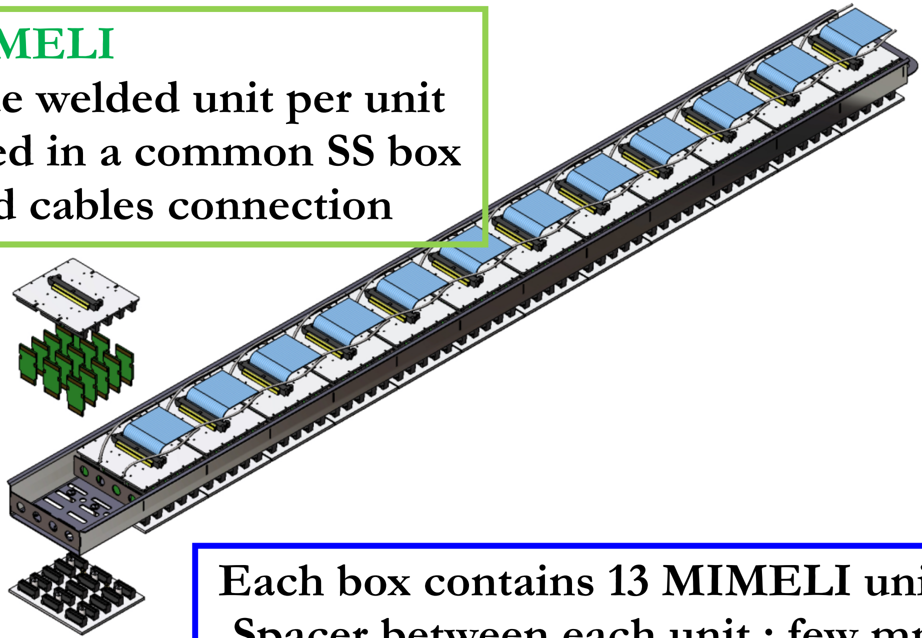
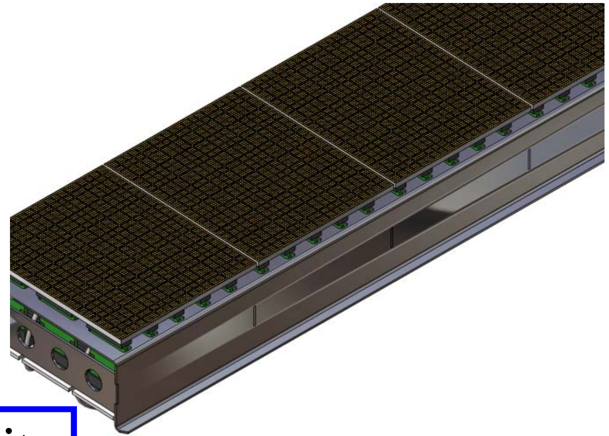
# MIMELI implantation and positioning

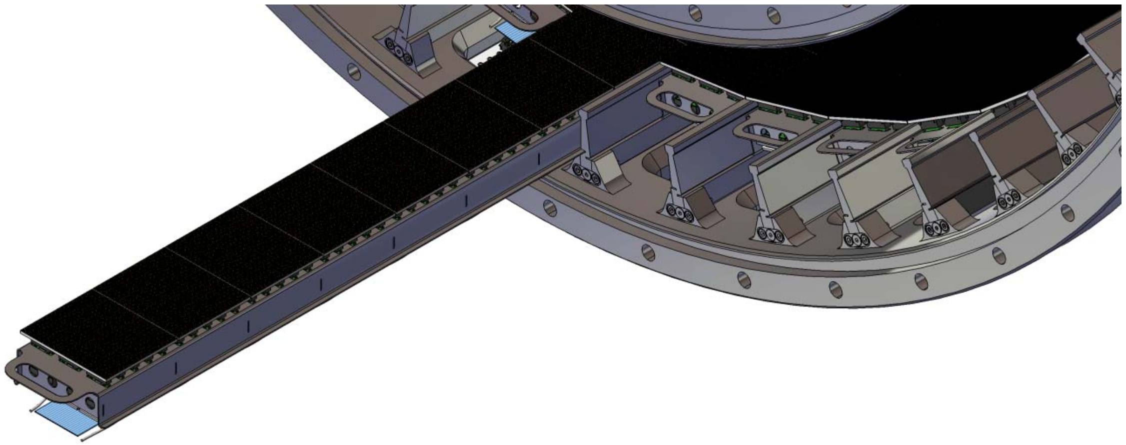


MIMELI
1/ µMesh and anode welded unit per unit
2/ 13 units assembled in a common SS box
3/ electronics and cables connection





Each box contains 13 MIMELI units
Spacer between each unit : few mm
Box length close to 1 m
Active area closed to 95%



Boxes precisely mounted on SS rails inside the cryostat
Boxes are completely immersed inside LXe
17x2 boxes per half barrel
Need additional 2m insertion space

R&D required for integration and for connection

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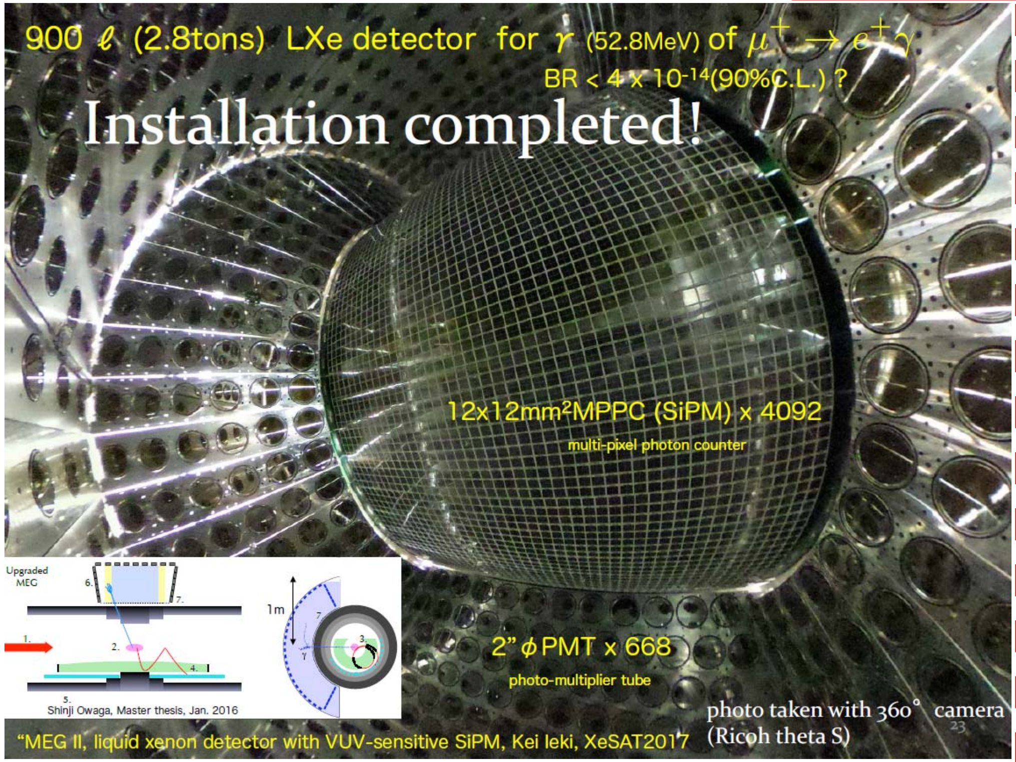
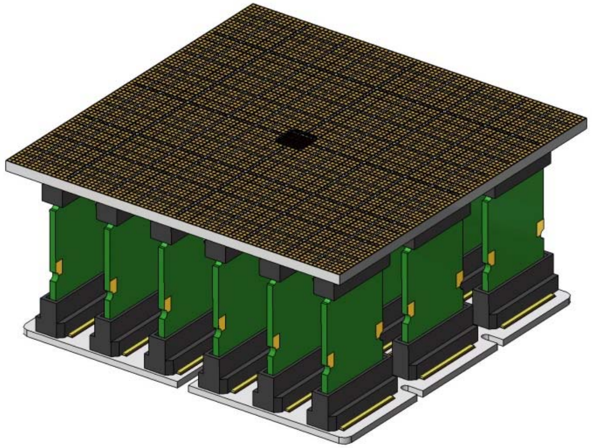
# MPPC for XEMIS-HT light detectors

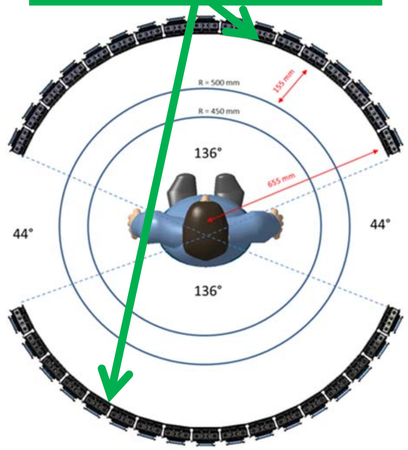
pôle imagerie défi 10 ps

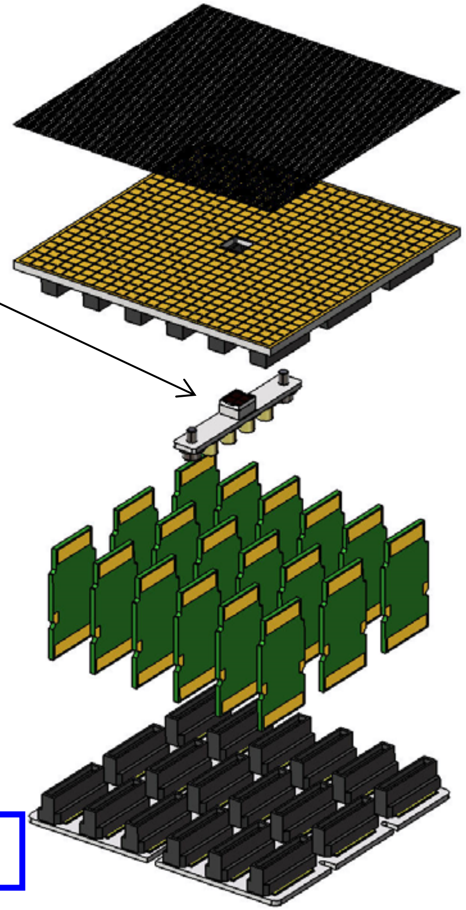
MPPC on anode

## 2 options

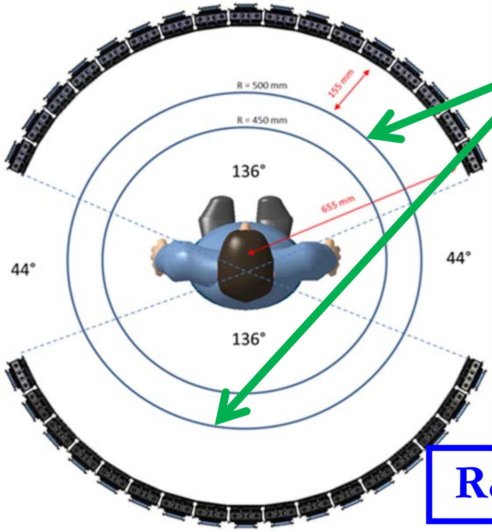




MPPC inserted "inside" IMELI




MPPC on cathode

Very good light detection for :

prompt/delayed time separation
PET-TOFPET monitoring
perfect n/γ identification

R&D required with mechanics, electronics and DAQ

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# On-line monitoring of the PGs with XEMIS-HT

Overall efficiency ~ $\varepsilon_{Accep}$ x $\varepsilon_{Cal}$ x $\varepsilon_{Compton}$
~ 50% x 15%x 33%

Safety factor for Compton tracking efficiency

Raw estimation : $\varepsilon_{PGs}$ ~ 2.7 % feasable

It means, with $10^n$ C ions on tumor, ~ 5.4 $10^{n-5}$ PGs detectable and coming from the last mm

**With 2° of angular resolution, mm resolution on the beam (1D) could be achieved from n ~ 7**

XEMIS2 DAQ for the charge read-out will follow :
- 900 PU cards
- 10 DAQ-FPGA interfaced to x86 platform

**R&D required with electronics and DAQ for MPPCs, with on line analysis and tracking for imaging**

- Beam inside patient could be on-line (1s) monitored with XEMIS-HT !!!
- First study very impressive and positive
- New partners are very welcome to start XEMIS-HT advanced feasibility studies

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