



**GDR** Groupement  
de recherche

**MI2B** Outils et méthodes nucléaires  
pour la lutte contre le cancer

# Pôle méthodes et instruments en imagerie biomédicale Highlights

Marc-Antoine Verdier (IJCLab), Mathieu Dupont (CPPM)

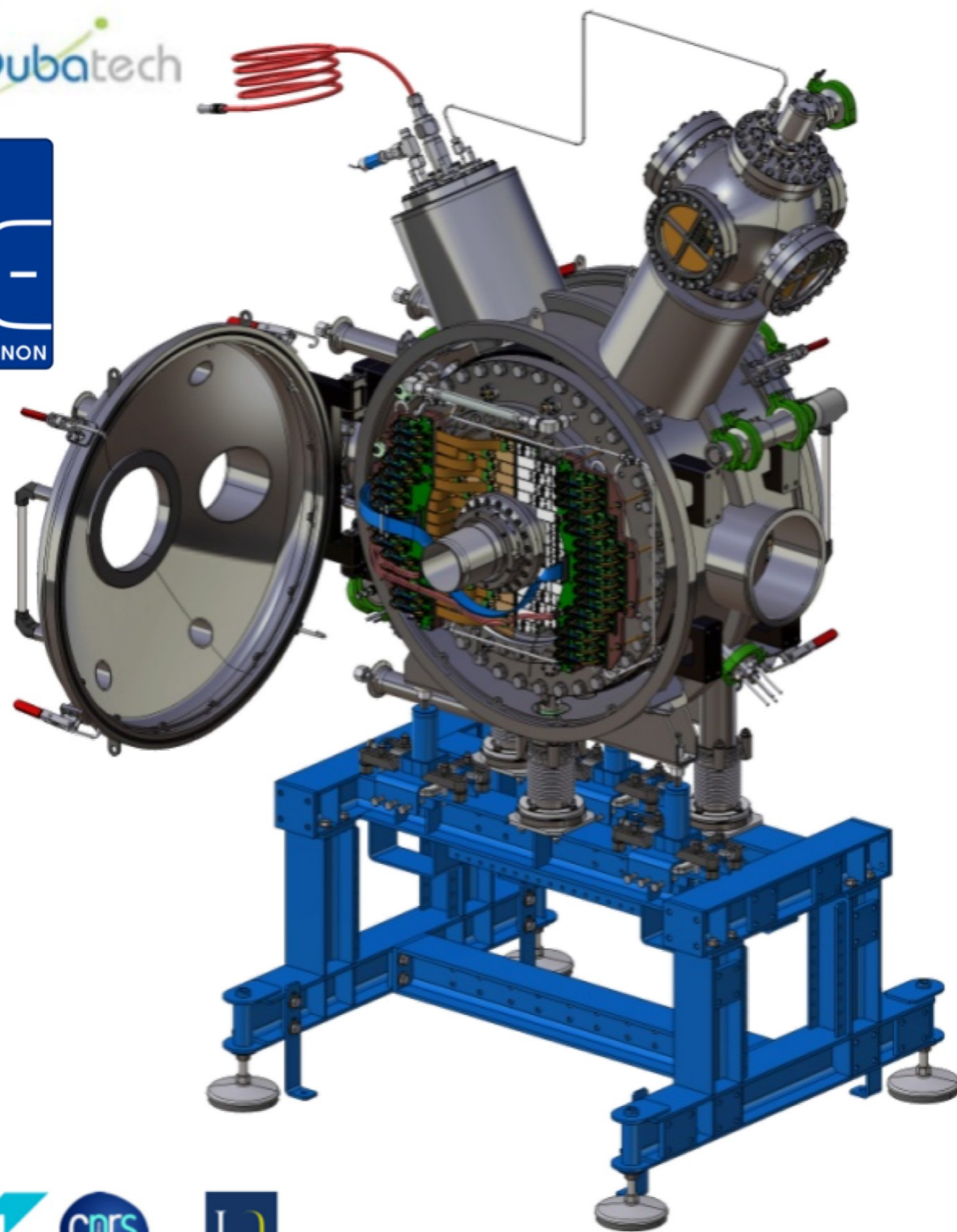
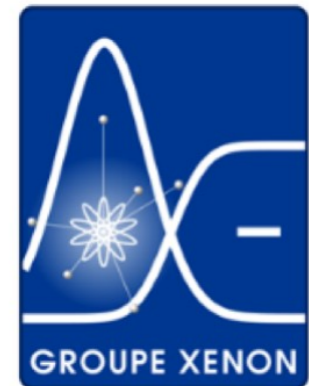
AG MI2B  
27-28 septembre 2021

# Présentations

- Floriane Cannet (CPPM) : Etude longitudinale de l'effet de différents traitements pour le carcinome hépatocellulaire chez la souris assistée par l'imagerie à rayons X
  - Laurie CAPPELLUGOLA (CPPM) : Modelisation of light transmission through surfaces with thin film optical coating in Geant4
  - Enrique Muñoz (IP2I) : Enhancement of Compton imaging of polychromatic sources through spectral reconstruction
  - Safaa Tahri (LTSI) : Image and dose uncertainties of a deep learning method for prostate MRI-only radiotherapy
- **Annonce : Organisation d'un workshop sur l'imagerie Compton : 30/11 – 01/12 au CPPM (indico à venir)**



Subatech



Depuis 80 ans, nos connaissances  
bâtissent de nouveaux mondes



## XEMIS2

Jean-Pierre Cussonneau ([jean-pierre.cussonneau@subatech.in2p3.fr](mailto:jean-pierre.cussonneau@subatech.in2p3.fr)),  
Dominique Thers ([dominique.thers@subatech.in2p3.fr](mailto:dominique.thers@subatech.in2p3.fr))  
et al.,

**Assemblée Générale  
27-28 Septembre 2021**

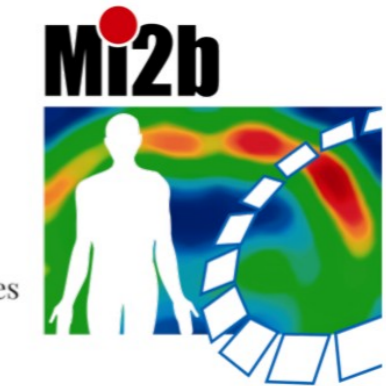


UNIVERSITÉ DE NANTES





# Thèses soutenues sur XEMIS2



**Debora Giovagnoli**

Image reconstruction for three-gamma PET imaging

Données simulées Geant4

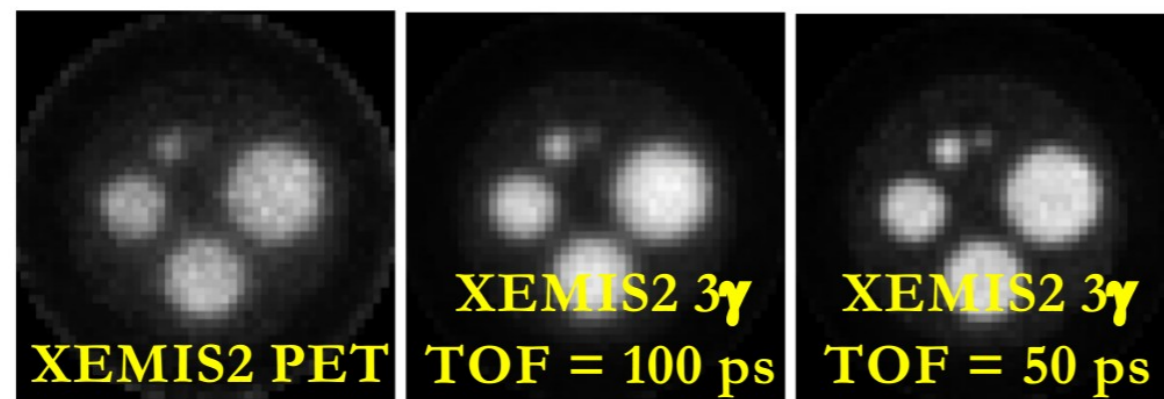
Reconstruction CASToR

Sphères chaudes rayon 2, 4, 8, 10, 12 mm

<sup>44</sup>Sc fixé avec contraste 15 sur fantôme

20 kBq, temps de pause 20 mns

Reconstruction ML-EM



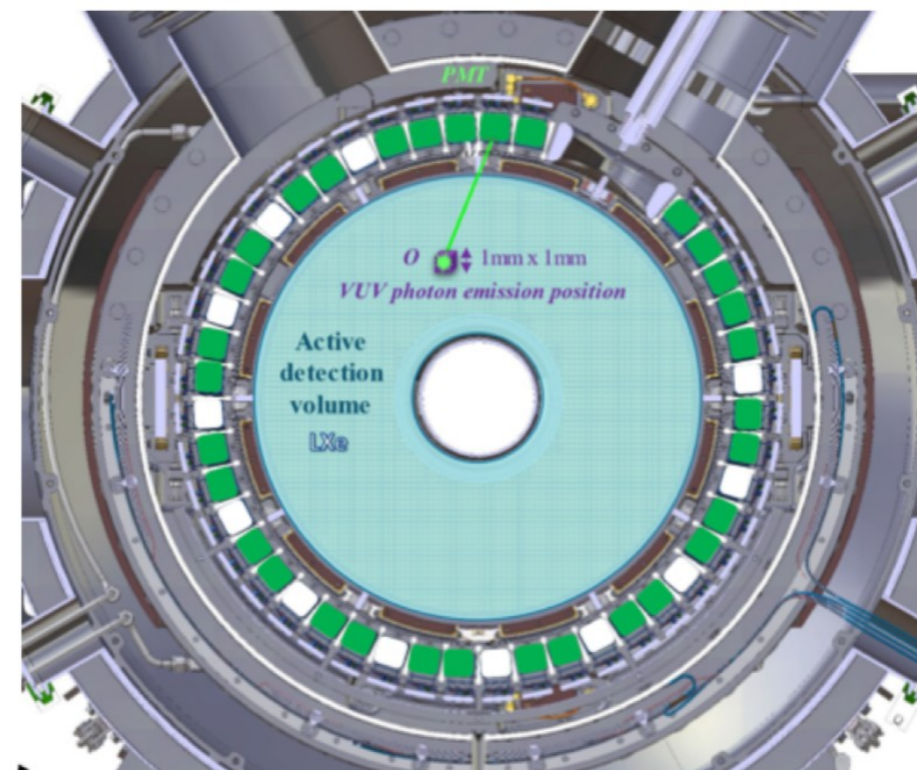
Bonnes images pour les 3 modalités

Code de reconstruction disponible



**Yuwei Zhu**

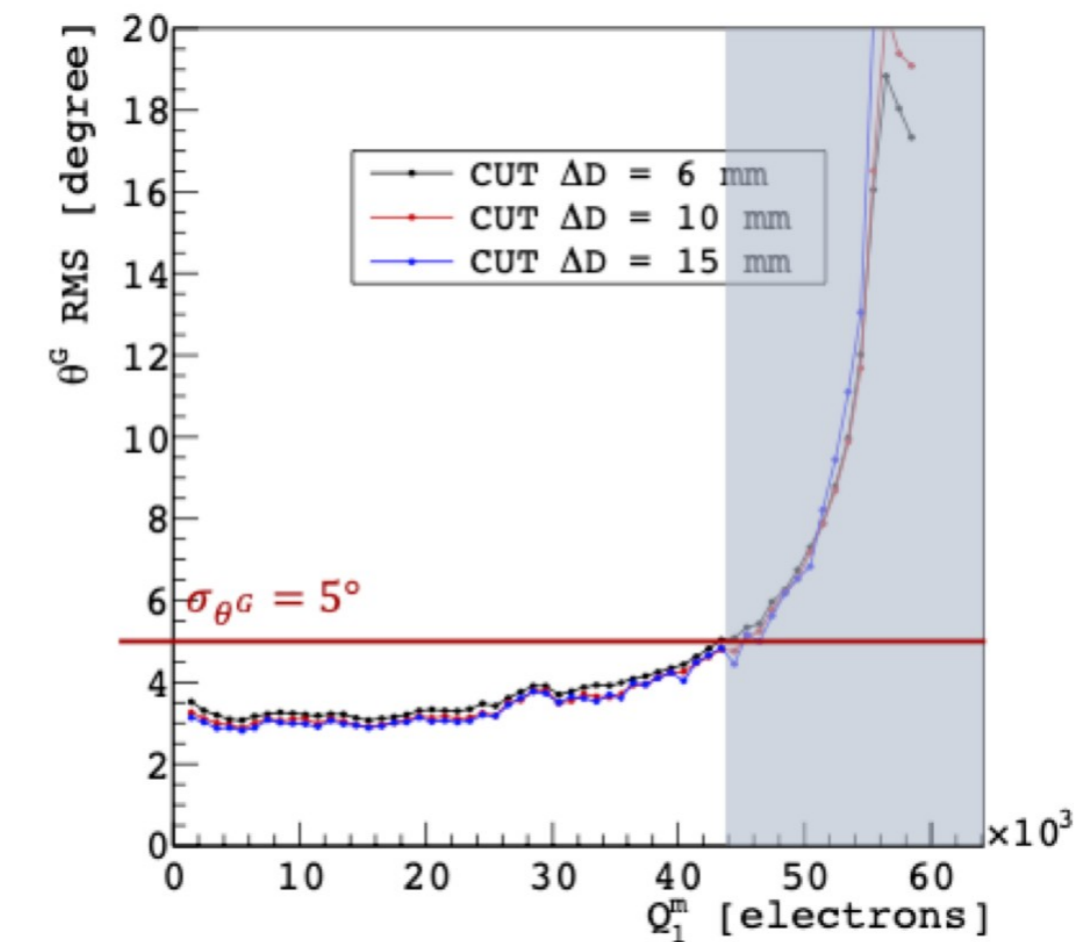
Développement de la caméra Compton au xénon liquide XEMIS2 pour l'imagerie 3-gamma: études et optimisation des mesures de la lumière de scintillation



La couverture en surface de photo-détecteurs permettra l'image à 20 kBq  
L'activité pourra être augmentée en augmentant la surface instrumentée

**Yajing Xing**

Études et optimisation de la mesure du signal d'ionisation dans la caméra Compton au xénon liquide XEMIS2 pour l'imagerie 3gamma



Résolution angulaire proche de 3° sur un large domaine angulaire



## Installation/qualification de XEMIS2 au CHU-CIMA de Nantes



conceived and developed @ SUBATECH



Installation @ Nantes CHU

**Mobilisation importante en 2021-22 (~ 10 ETPs)**

**Objectif Gestion du projet :**

**Installation jusqu'en mars 2022**

**Exploitation à partir d'octobre 2022**

**Assemblée Générale GDR MI2B, 27-28 Septembre 2021**



# The CLaRyS collaboration

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- 4 labs

- 3 IN2P3 labs: CPPM, IP2I, LPSC + CREATIS (Biomedical imaging lab in Lyon)

- Objectives

- Contrôle en Ligne de l'hadronthérapie par détection de Rayonnements Secondaires

- Current projects

- Gamedi: collimated and Compton cameras with TOF
- CLaRyS-UFT (on-going "Physique Cancer" project): TOF-Compton camera with ultra fast timing (UFT)
- PGPI: PG counting in a few detectors around the patient
- TIARA (starting "Physique Cancer" project): PG emission vertex reconstruction by means of TOF

- Strengths

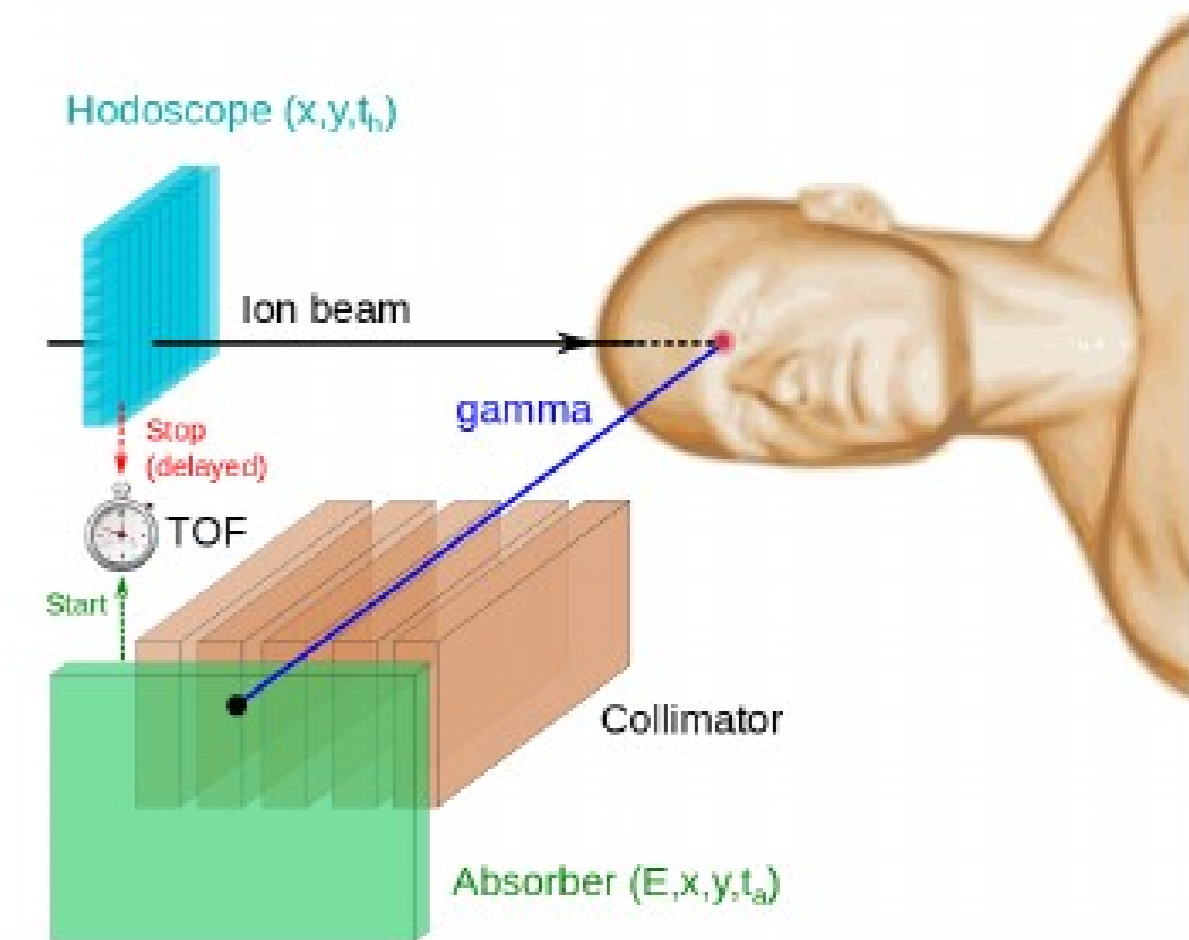
- Synergy between the projects
- Same acquisition system (AMC40 board,  $\mu$ TCA standard)
- Common Monte Carlo simulations tools (Geant4, GATE)



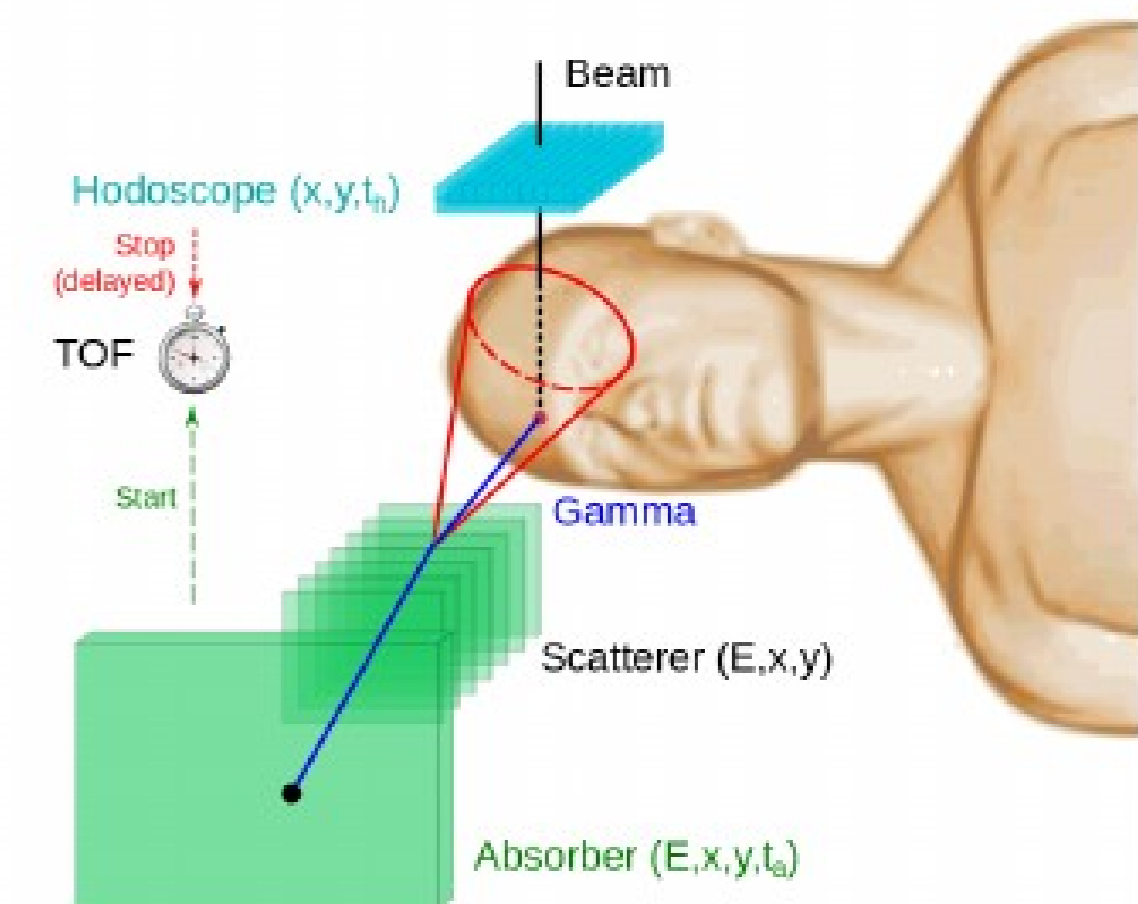
# The Gamedi projet

- The Gamedi project: Gamma cameras for medical applications
  - Multi parallel-slit camera (MPS) + Compton camera (CC)
  - Compton camera also considered for nuclear imaging (diagnostics)
- Positioning wrt state of the art
  - MPS:
    - Similar efficiency as the one of KES but measurement of the whole PG profile
    - Background reduction with TOF
  - CC
    - Hodoscope: Line-cone reconstruction + TOF
    - Perspectives of UFT (project CLaRyS-UFT)
    - Use of relatively thick silicon detectors (2 mm)
    - Perspective of detection efficiency enhancement (factor  $\sim 50$  wrt collimated cameras)

## Multi parallel-slit cam.



## Compton camera





# The Gamedi projet

- **Demonstrators**

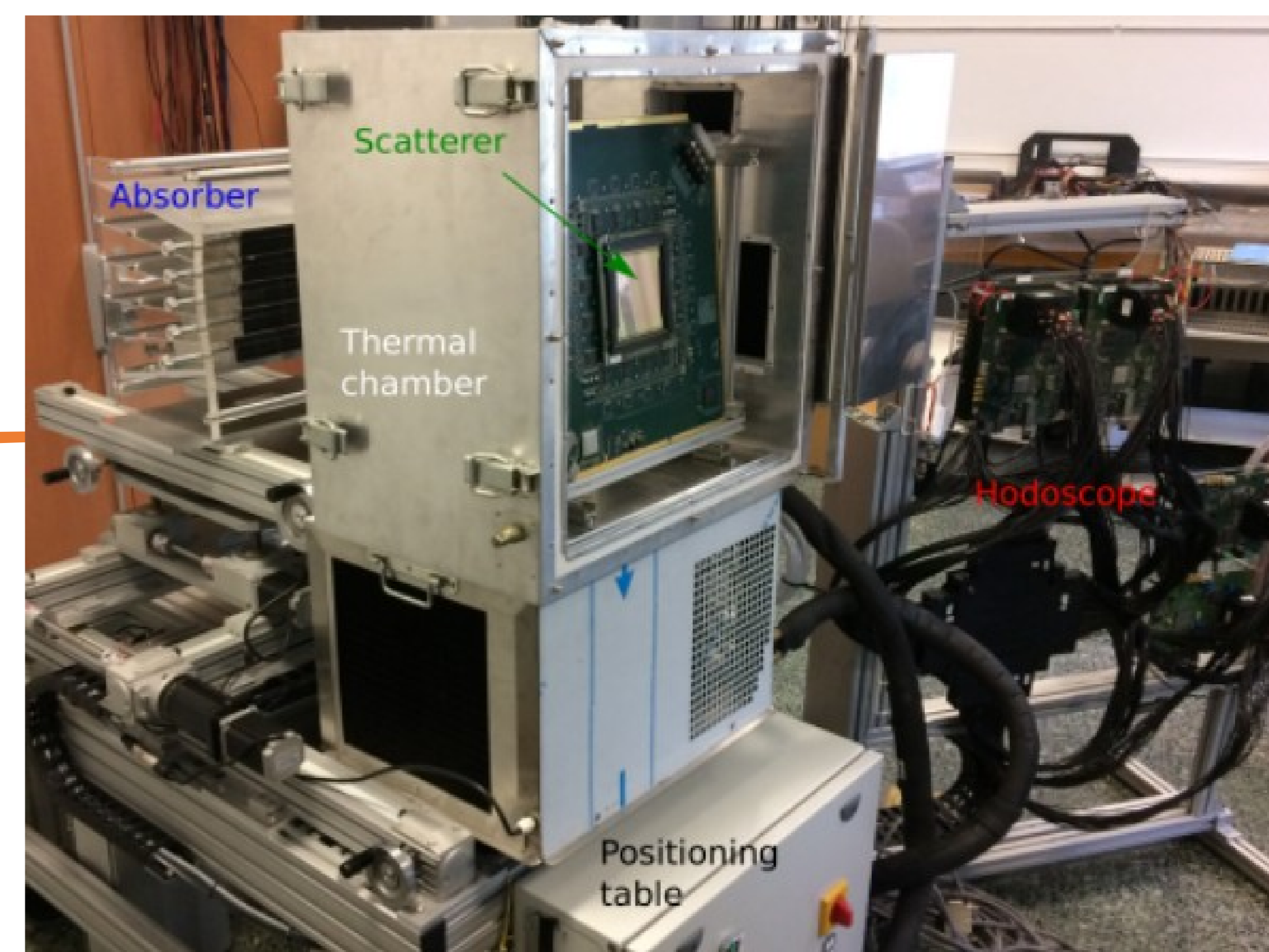
- Common beam hodoscope (scintillating fibers) and absorber (BGO)
- Common acquisition system and software
- Scatterer of the CC: 7 double sided silicon detectors
- Collimator of the MPS: Tungsten alloy

- **Current status**

- “Small hodoscope” and absorber characterized (lab+in-beam tests)
- Planned for 2021: CC scatterer firmware + integration in the CLaRyS acquisition

- **Perspectives**

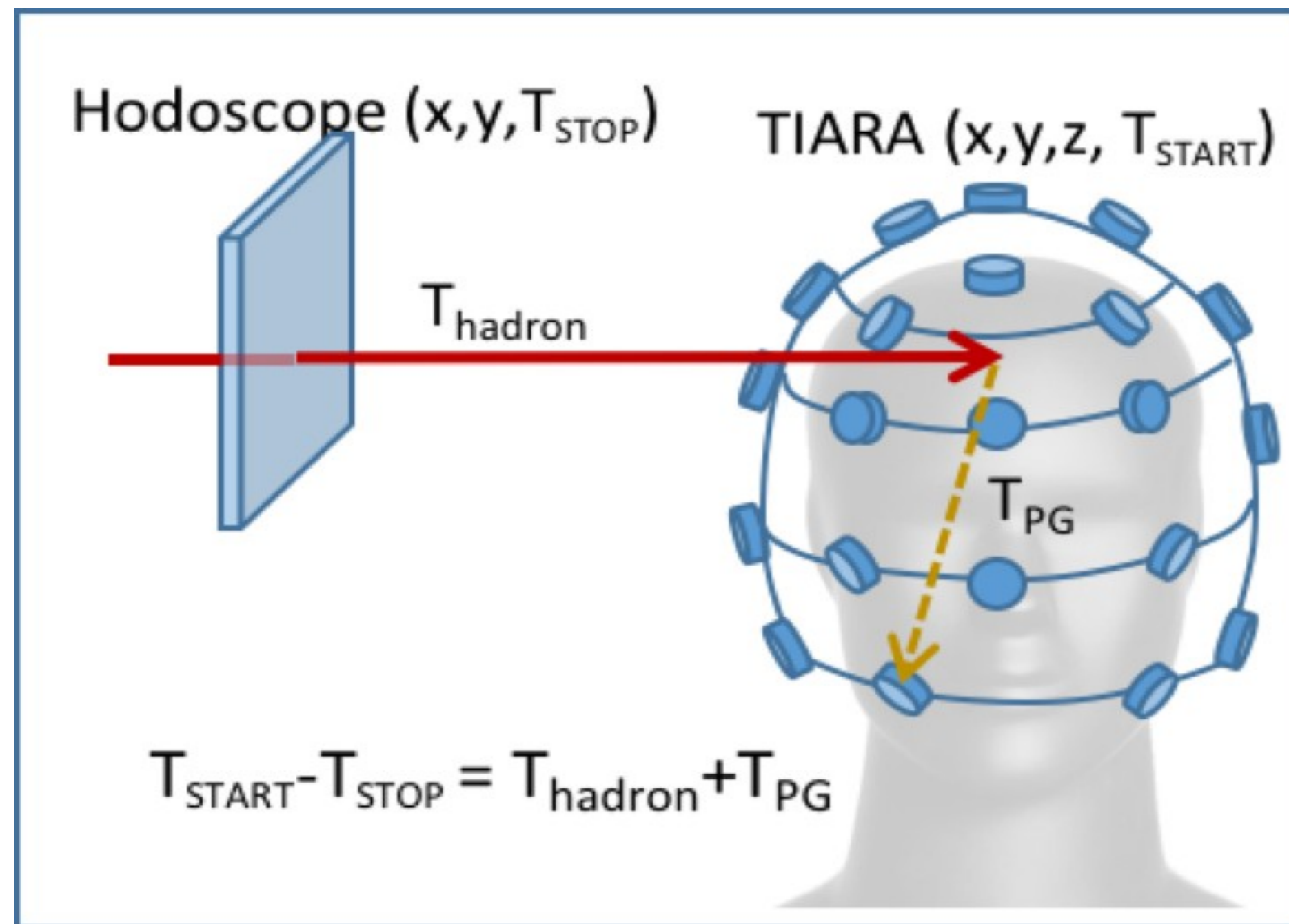
- Instrumentation
  - Further instrumentation developments within Oreste Allegrini's PhD (Fall 2022)
  - Beyond 2022: instrumentation developments questionable (lack of (mainly human) resources)
- MC simulations
  - Further collaborations with CREATIS, LPSC, CPPM, IFIC (Valencia), Subatech (XEMIS) to investigate/further optimize CC (and PGPI, TIARA...)





# TIARA: TOF Imaging ARrAy

(3D imaging of PG vertex through the exclusive measurement of TOF)



## Pixel detector: Cherenkov radiators + SiPM

- TOF resolution better than 100 ps rms
- No energy measurement
- Excellent background rejection through
  - ✓ TOF
  - ✓ Cherenkov threshold

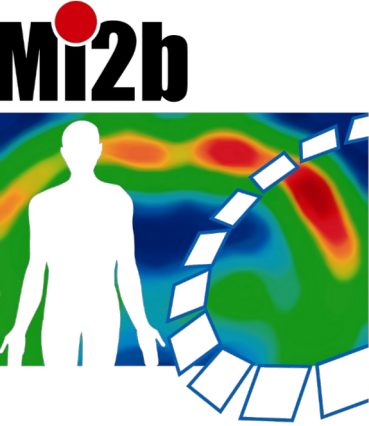
- 3D reconstruction will allow to obtain an image of the Prompt Gamma vertex distribution



# Projet TEMPORAL (2016 – 2021)

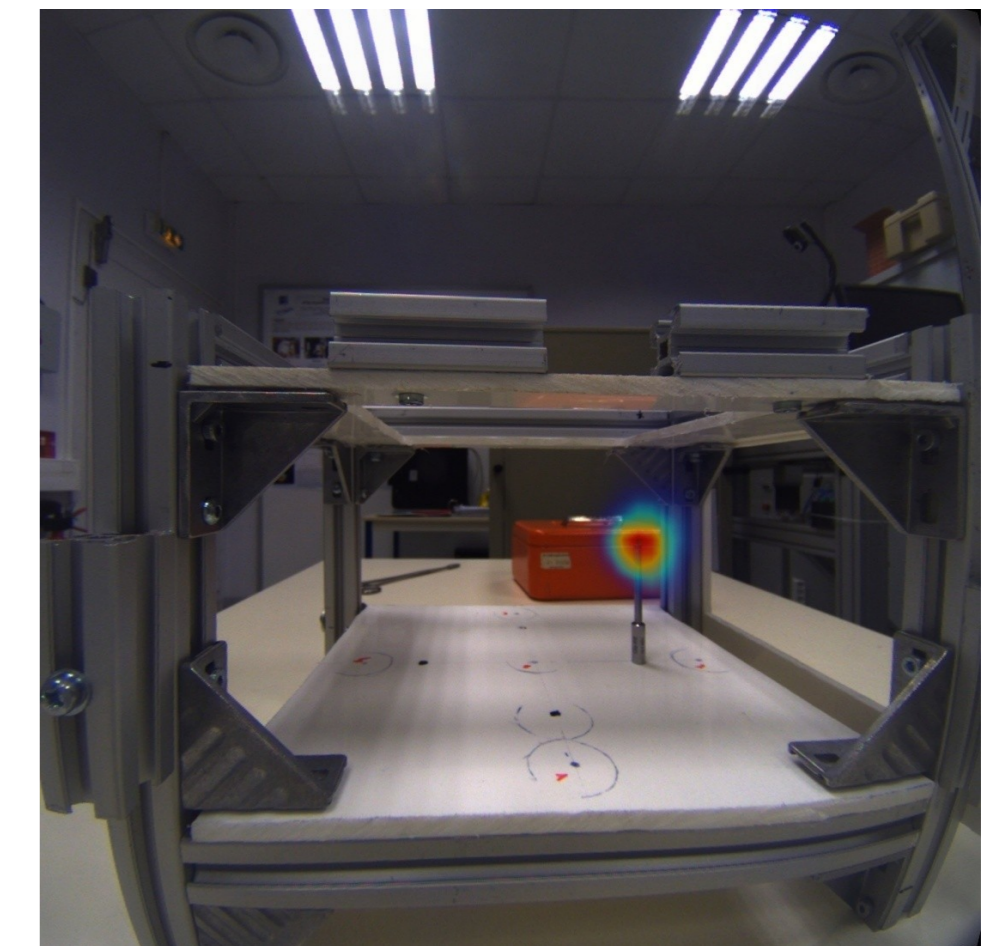
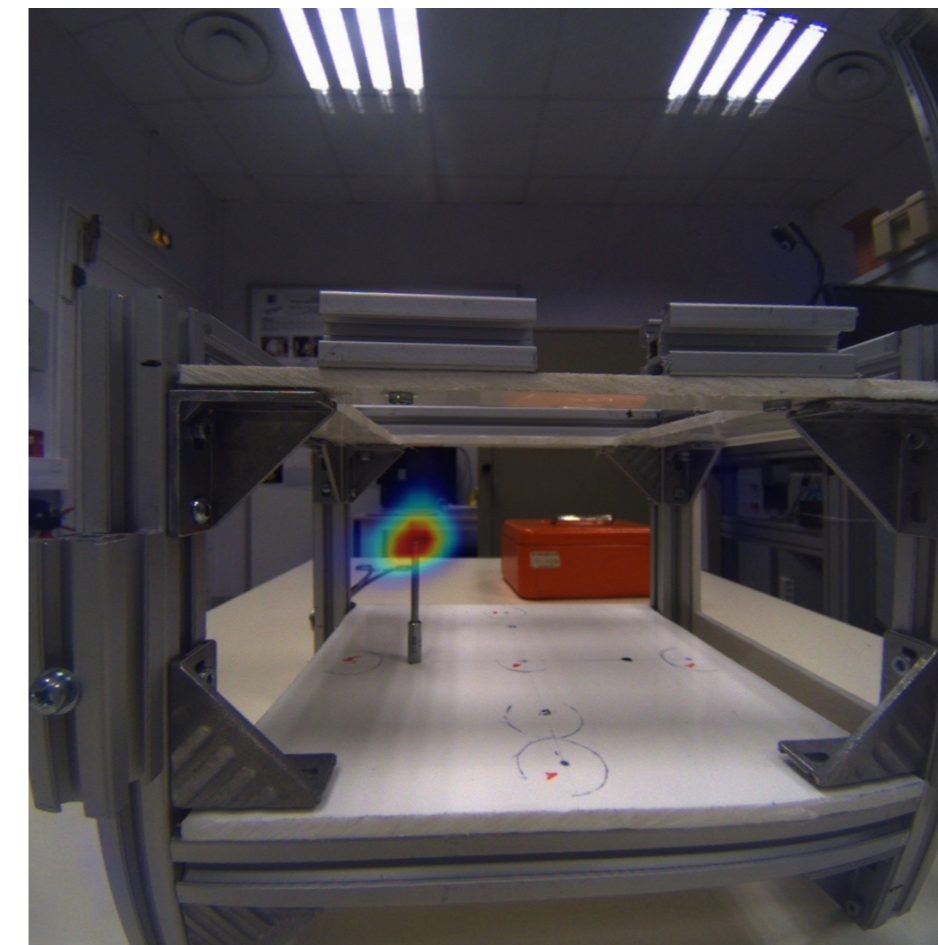
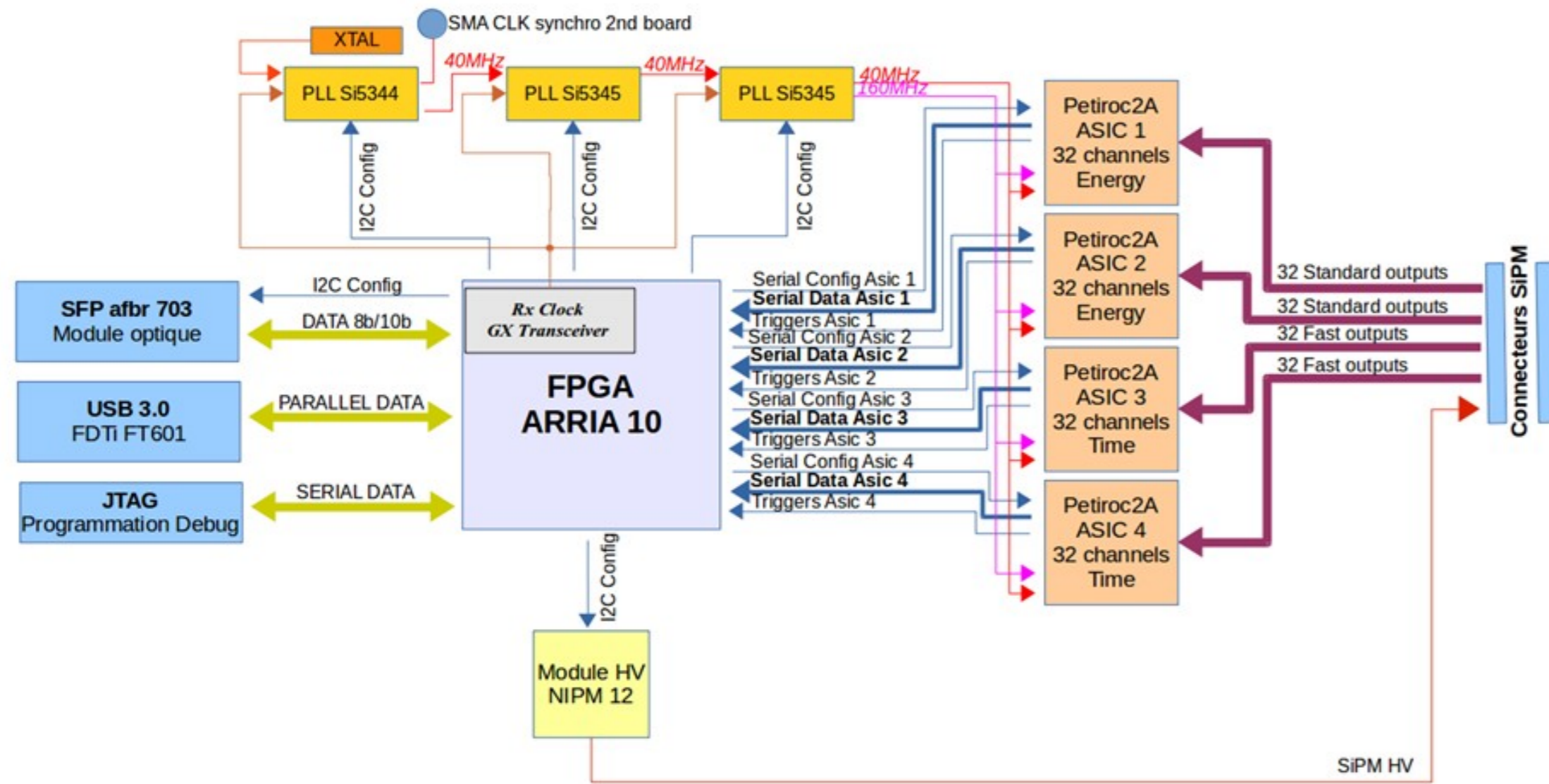
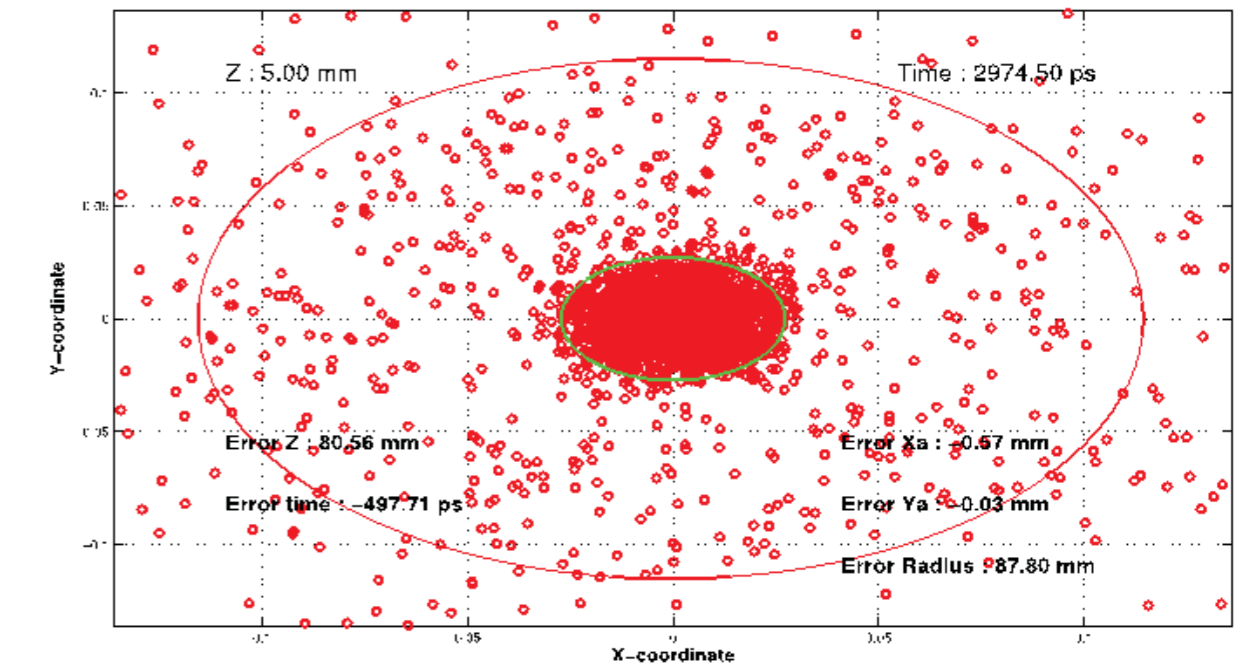
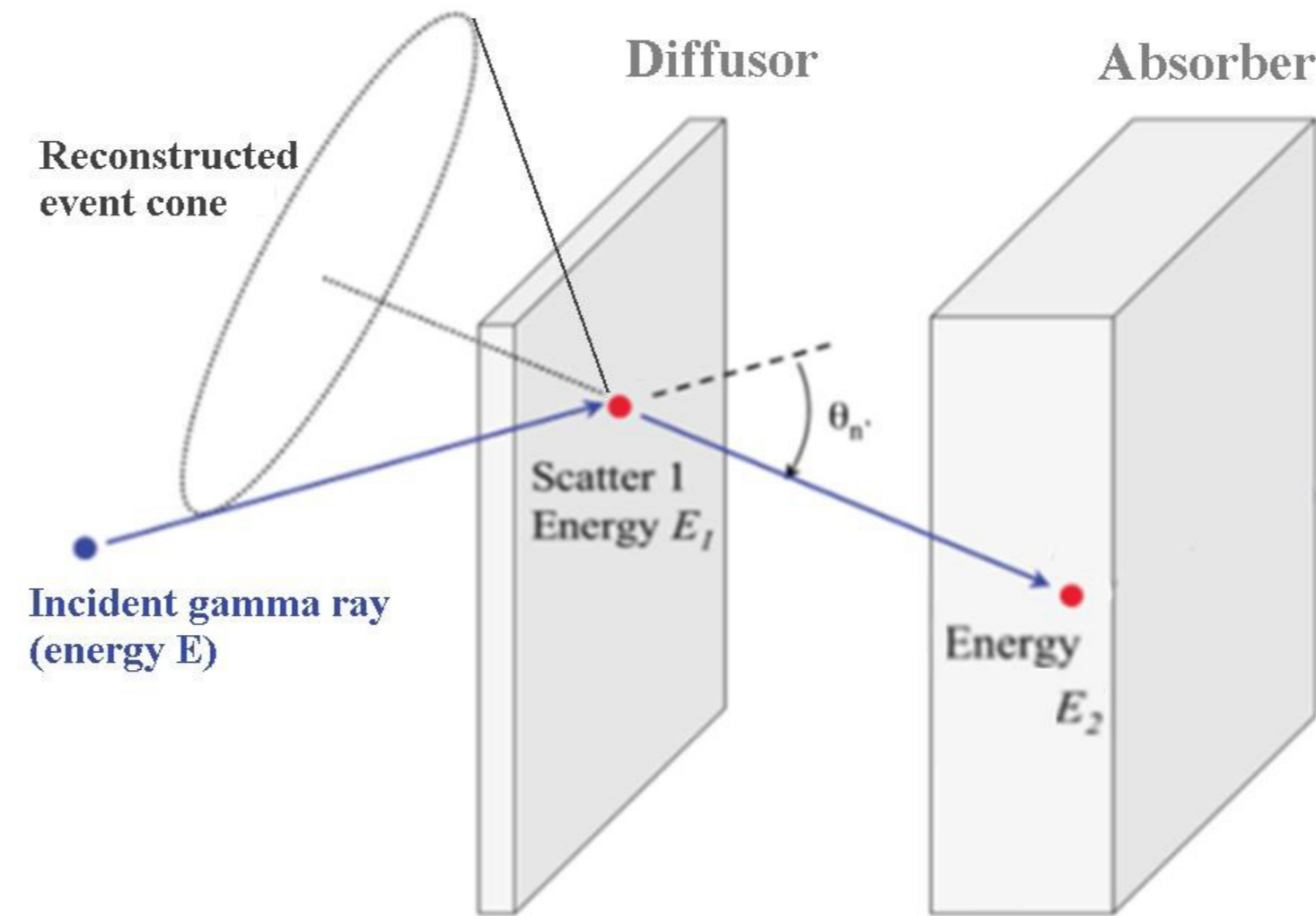


Depuis 80 ans, nos connaissances bâtissent de nouveaux mondes



## TEMPORAL

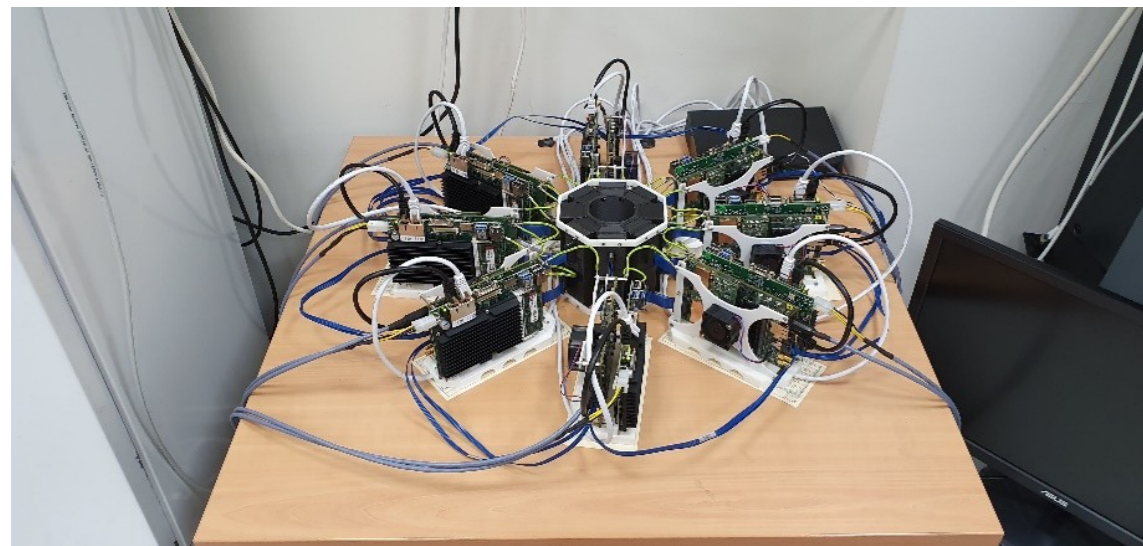
➤ Développement d'une caméra Compton pour le démantèlement nucléaire basée sur une méthode d'imagerie temporelle





**Question:** impact de l'approche instrumentale (choix technologiques) sur les performances des systèmes TEP précliniques ?

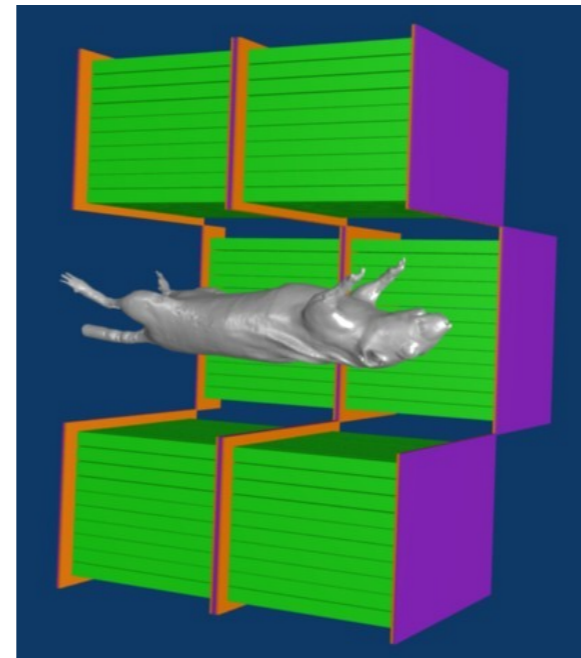
**Approche géométrique:**  
2D: approche dual layer



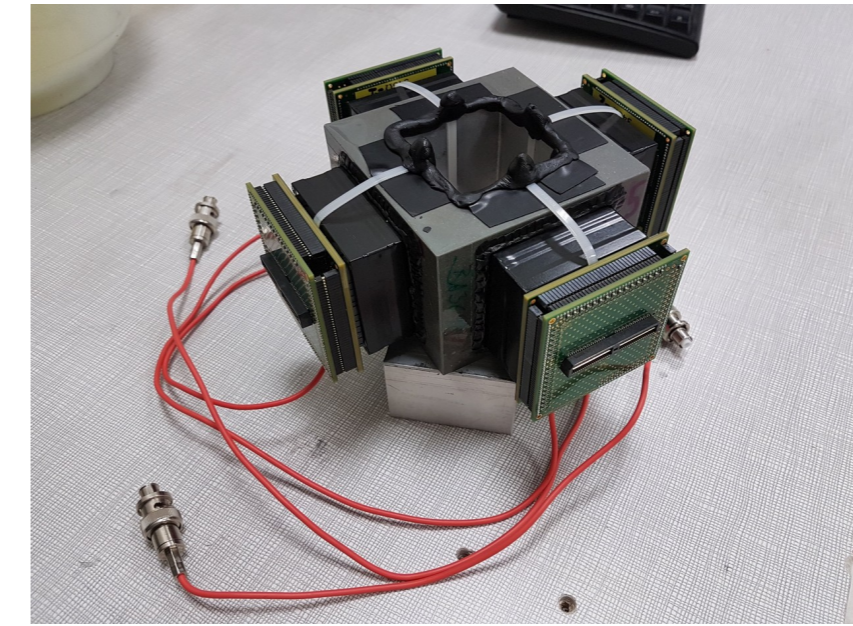
Projet DigiPET

Financement BPI - Région  
Partenaire Inviscan

**Approche géométrique:**  
2,5D: approche classique  
+ DOI (radiale ou axiale)

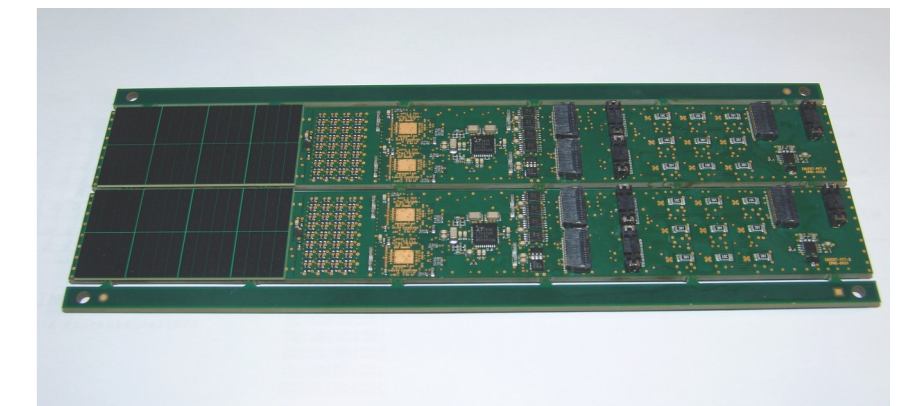
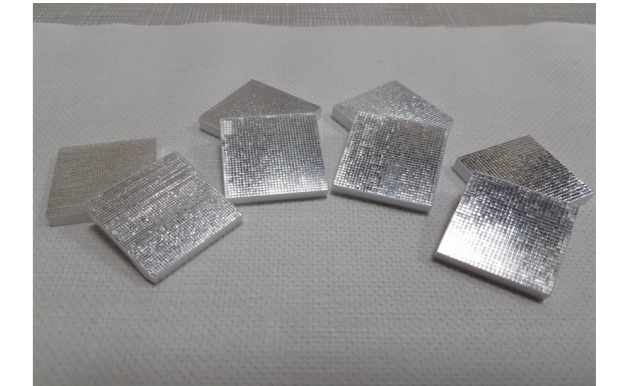


**Approche géométrique:**  
3D: bloc continu



Projet JackPET

**Compatibilité IRM**



Projet InsertPet

Financement CPER I2MT  
Collaboration ICube

Salvador S et al. 2009, 2010  
Fang X et al. 2010, 2011, 2012  
Ollivier-Henry N et al. 2010  
Brard E et al. 2013  
Brasse D et al. 2010, 2015  
Boisson F et al. 2017  
Brasse D and Boisson F 2019

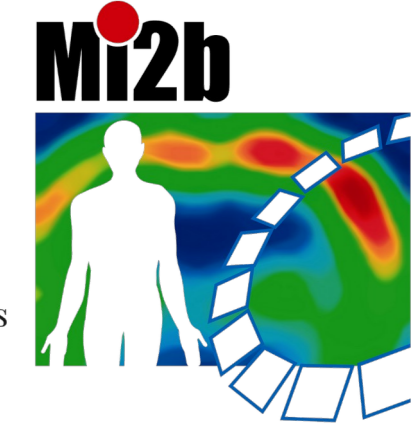
**Développement DAQ modulaire (ASICs IMOTEP + FPGA)  
Lecture MA-PMT & SiPM**

Vers la clinique : TOF (Défis 10ps), solutions instrumentales alternatives, IA



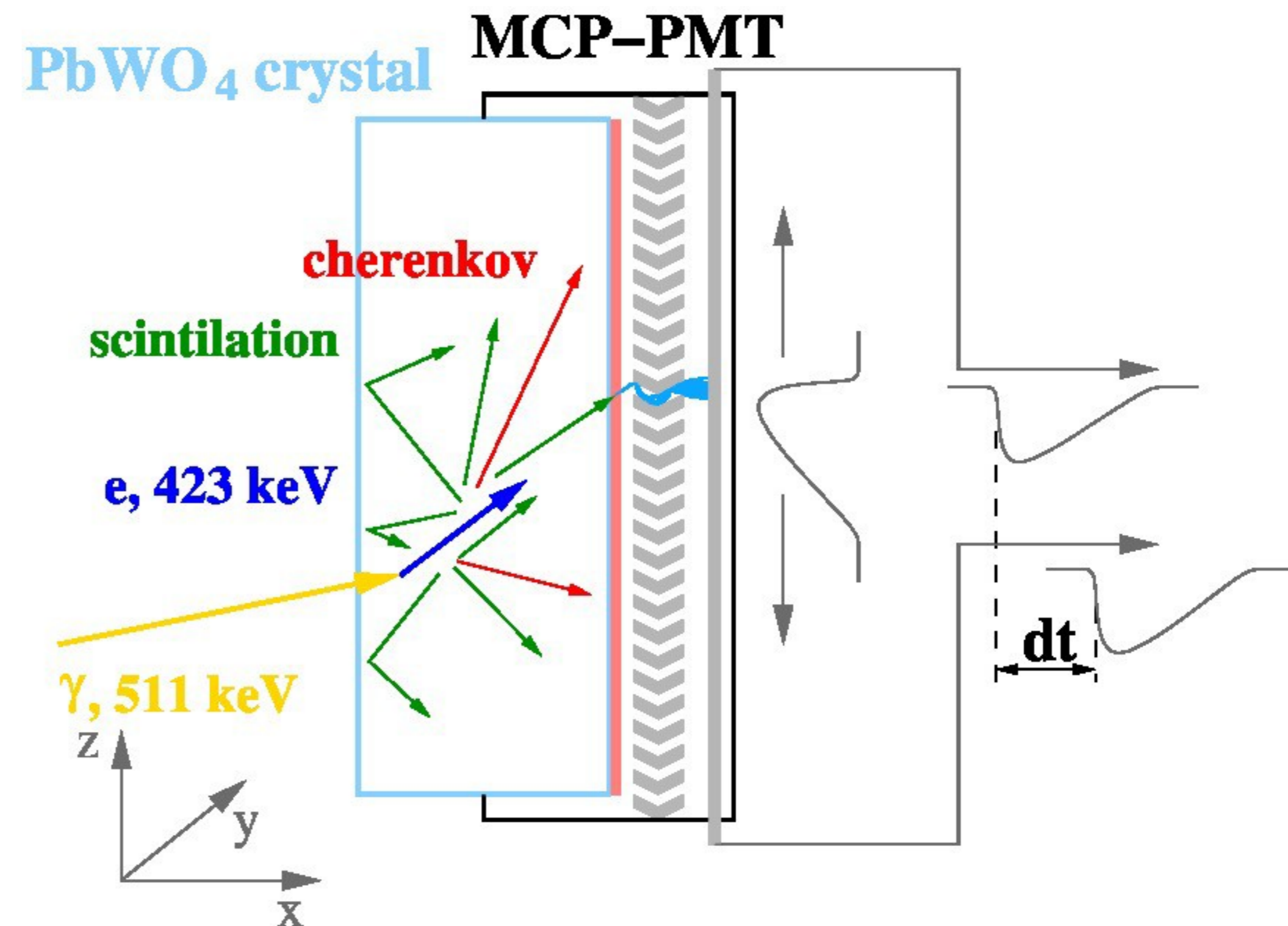


# Projet ClearMind (ANR 2019 - 2022)



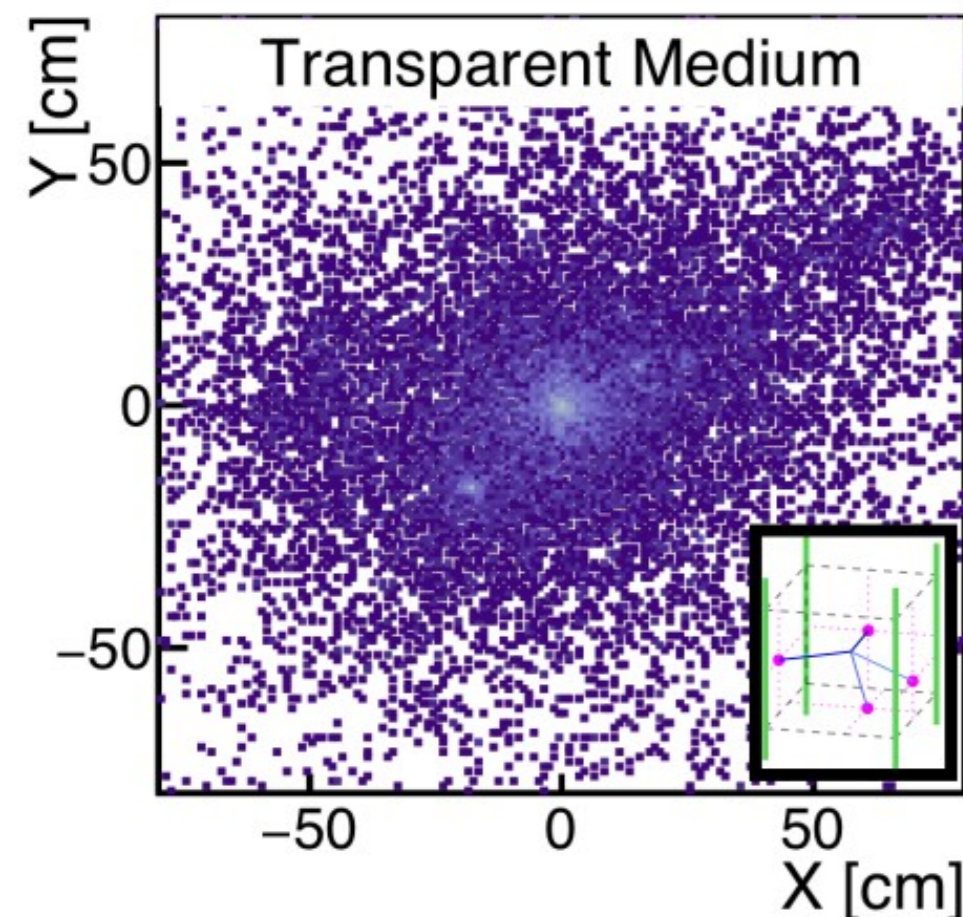
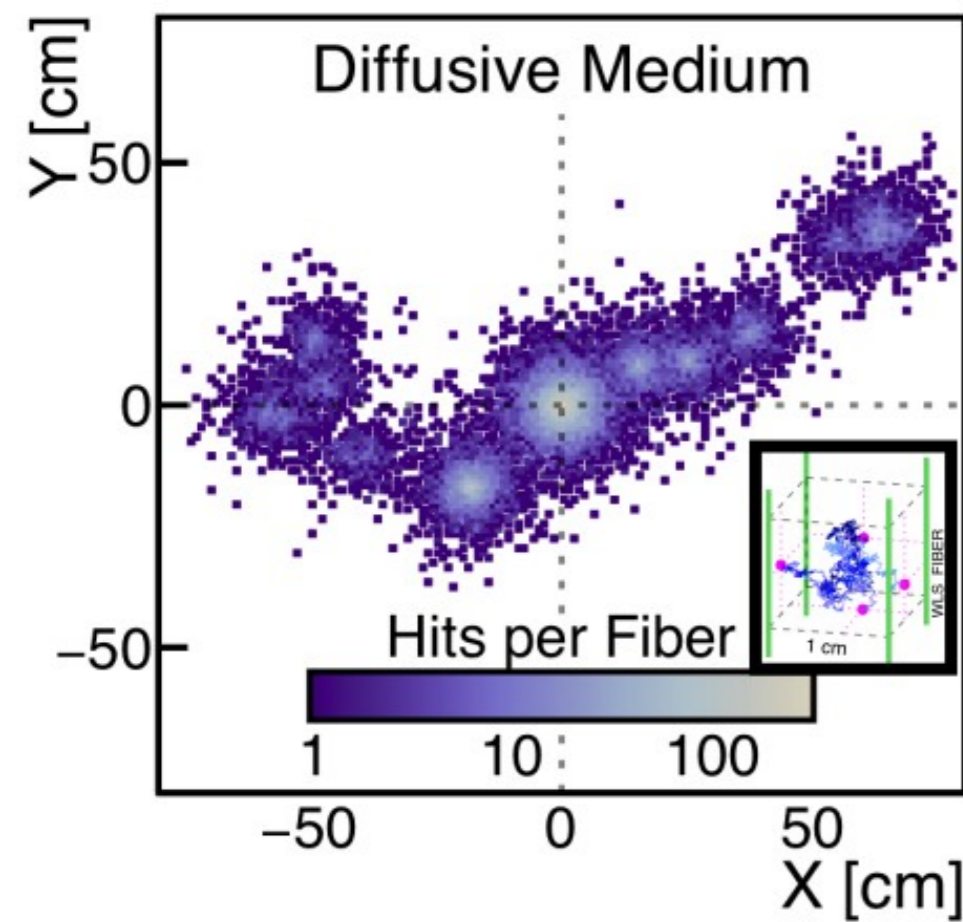
Développement d'un cristal « **scintronique** » pour les applications d'imagerie ultra-rapide de rayons gamma

- Détection des photons Cerenkov émis dans le  $\text{PbWO}_4:\text{Y}$
- Dépôt d'une photocathode ( $n \sim 2,7$ ) par évaporation directement sur la surface du cristal ( $n \sim 2,3$ )
- Amélioration de l'efficacité de collection optique sur la photocathode (**x4**)
- Encapsulation dans un tube multiplicateur à galette de microcanaux (MCP-MT)
- CRT  **$\sim 20$  ps FWHM** (hors MCP-MT)
- Simulation / validation sur tomXgam





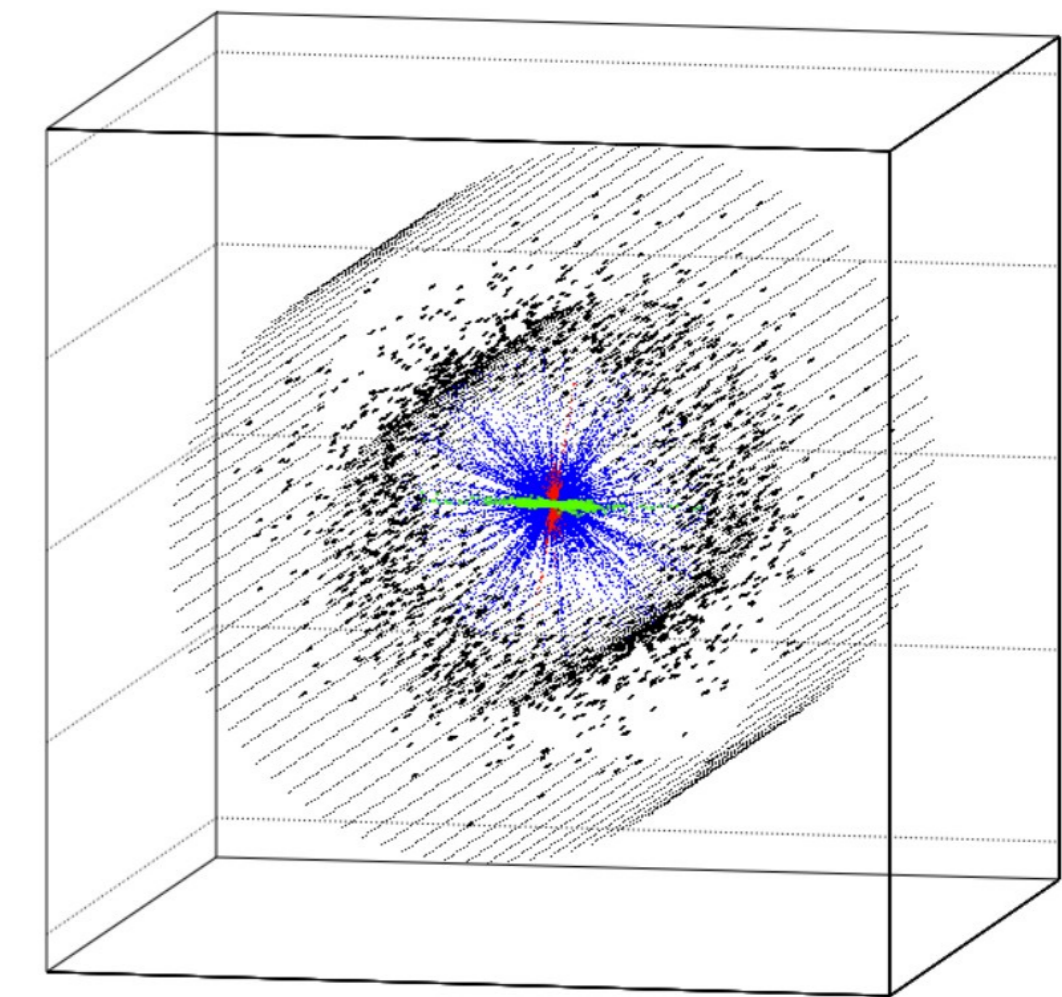
# LPET : Novel Positron Emission Tomography with Liquid Opaque Detection Technology



- Démonstrateur PET basé sur la technologie LiquidO [1]
- Scintillateur liquide opaque
  - Parcours moyen des photons optiques nul
  - Boule de lumière pour chaque interaction
- Lecture par un réseau de fibres WLS et SiPM
- Électronique de lecture rapide (Sampic)
- Reconstruction 3D des multiples Comptons
- Étude des possibilités multi-gamma ( $\geq 2$ , prompts et retardés)

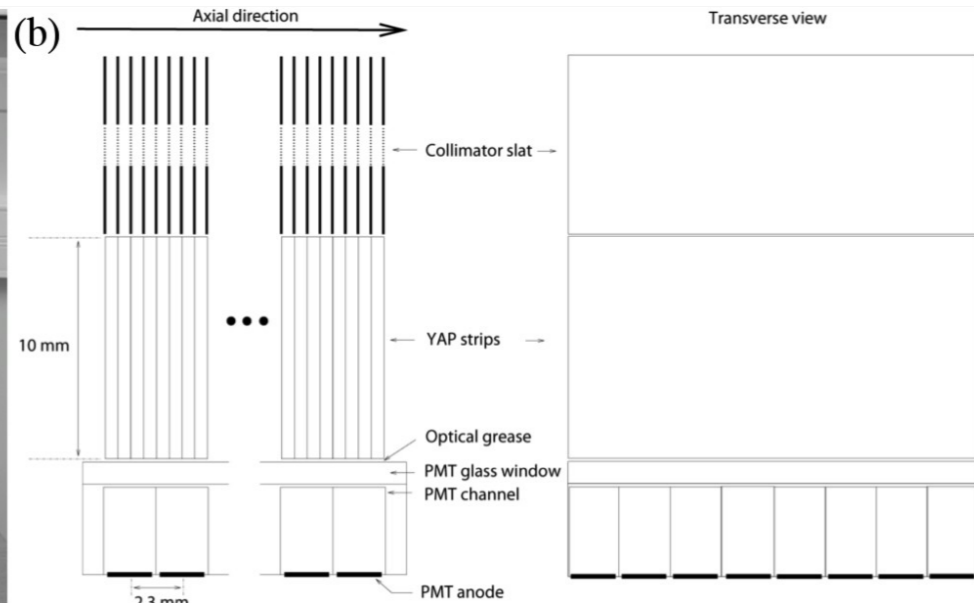
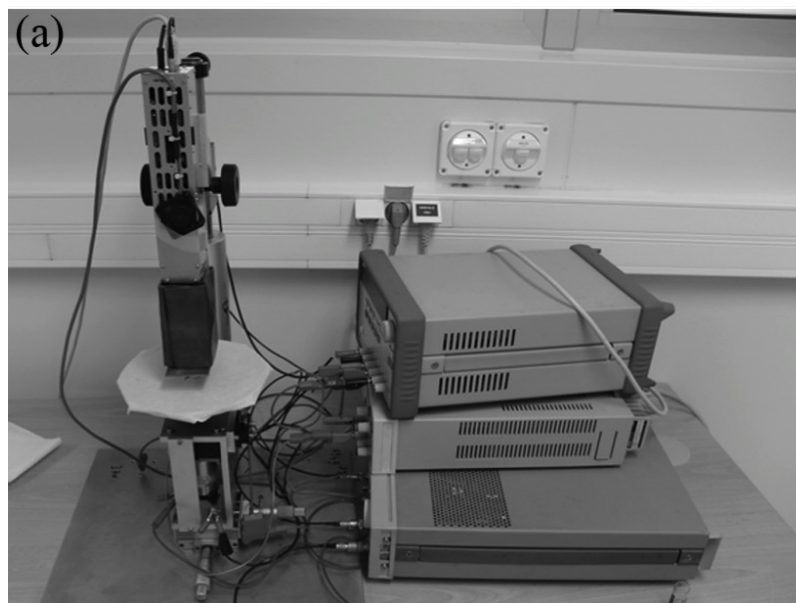
Projet ANR Tep-O-Tech 2022-2025 CNRS  
(IJCLab, IPHC et Subatech) et INSERM (LATIM)

[1] <https://arxiv.org/abs/1908.02859>

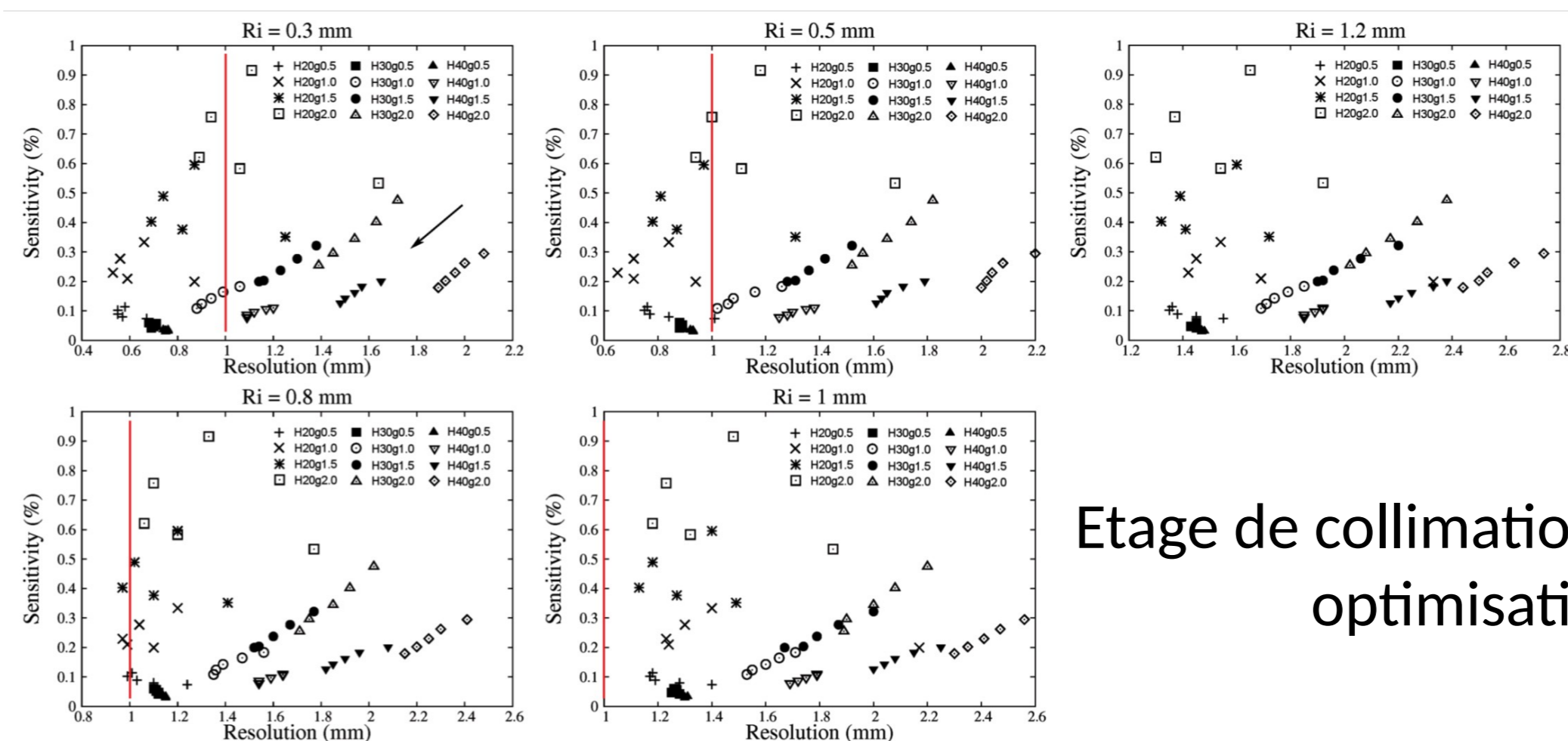




# Question: impact de l'approche instrumentale (choix collimation) sur les performances des systèmes TEMP précliniques ?



Premier prototype, rotation de l'ensemble du détecteur (crystal segmenté en 1D)



Boisson *et al.* 2011, 2015, 2016

Etage de collimation et résolution intrinsèque: optimisation des paramètres



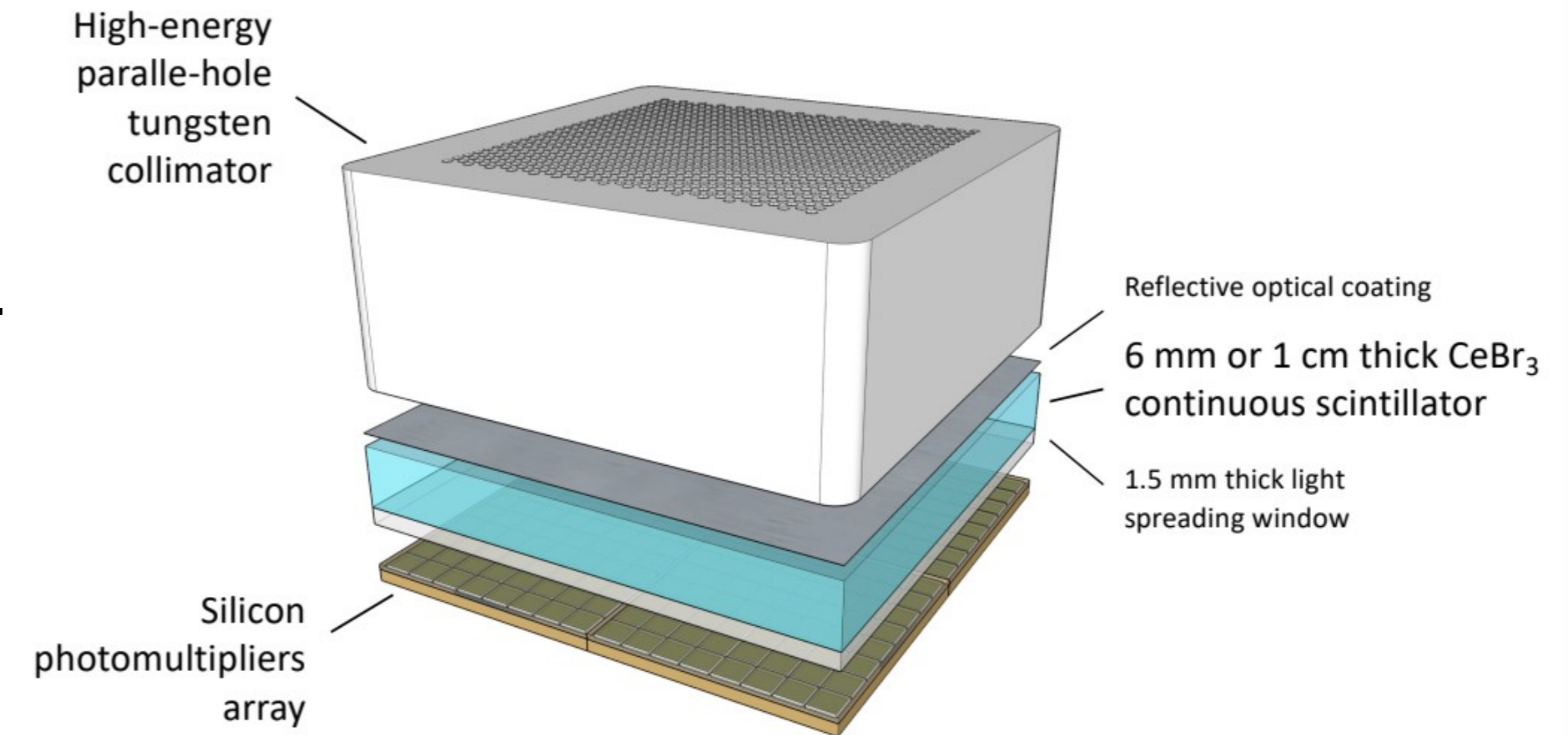
## Prototype actuel:

- 50 x 50 x 6 mm<sup>3</sup> CeBr3 monolithique (Scionix, Netherlands)
- H9500 MA-PMT
- DAQ (IMOTEP + FPGA)
- Collimation à lames parallèles (g=2mm, H=20mm)



# Thidos: Une gamma-caméra portable pour l'optimisation de la dosimétrie des patients pour thérapies par radio-iode des maladies de la thyroïde

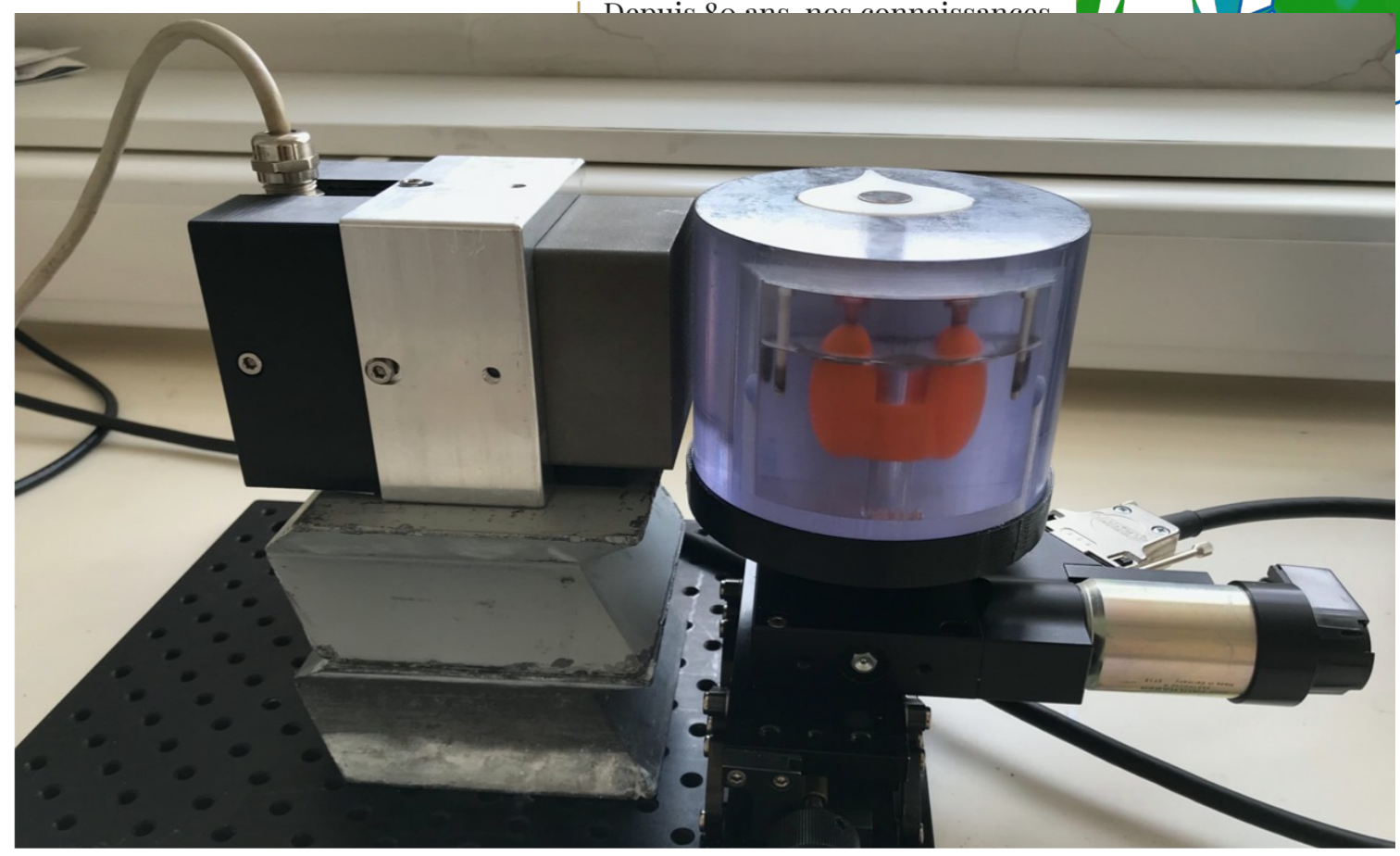
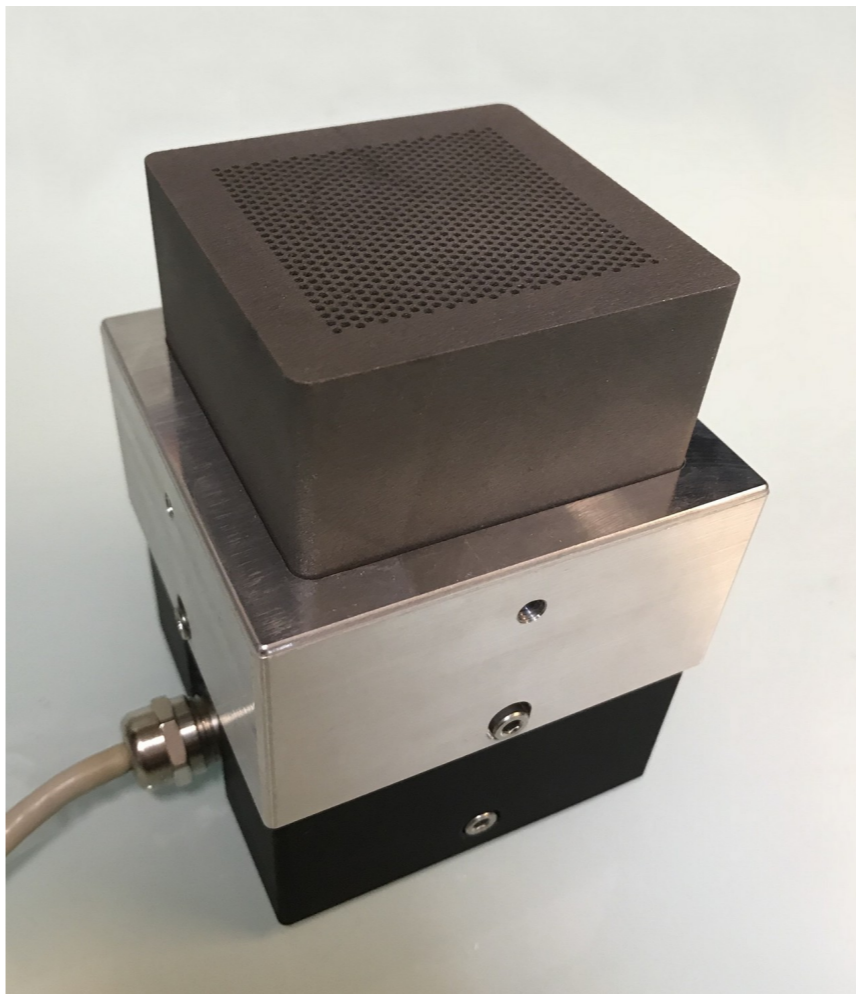
- Nouvelles approches instrumentales et méthodologiques :
  - 1) Conception, développement et calibration d'une gamma-caméra ambulatoire à haute résolution spatiale.
  - 2) Analyse de la fiabilité et de la qualité du calcul de la dose basée sur l'intégration de différentes données fonctionnelle, anatomique et pharmacocinétique.



With financial support from ITMO Cancer AVIESAN within the framework of the Cancer Plan (AAP Physicancer 2019-2023, THIDOS project)

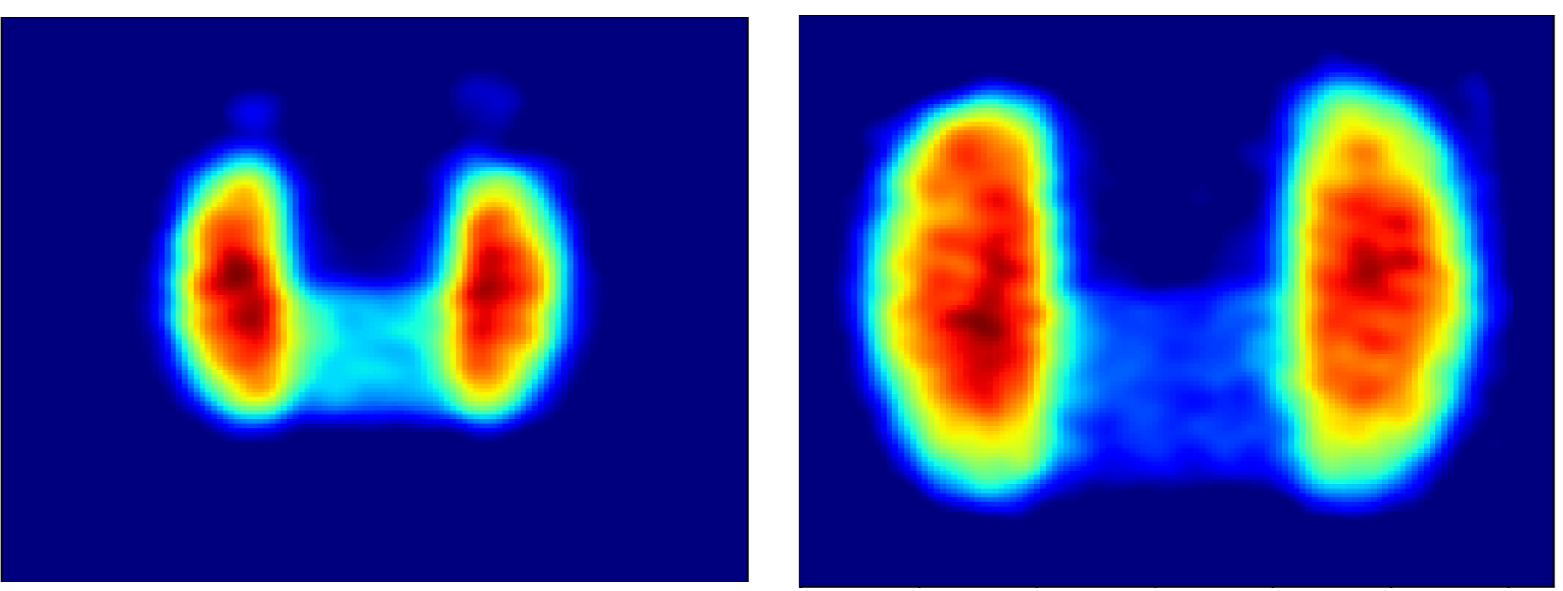


- 1er prototype
  - Champ de vue  $5 \times 5 \text{ cm}^2$
  - Scintillateur  $\text{CeBr}_3$  monolithique  $5 \times 5 \times 0.6 \text{ cm}^3$
  - Module de photodétection 256 voies MPPC  $3 \times 3 \text{ mm}^2$
  - Électronique 256 voies dédiée (LAL)
  - Collimateur à trous parallèles tungstène par impression 3D
- Validation sur fantômes

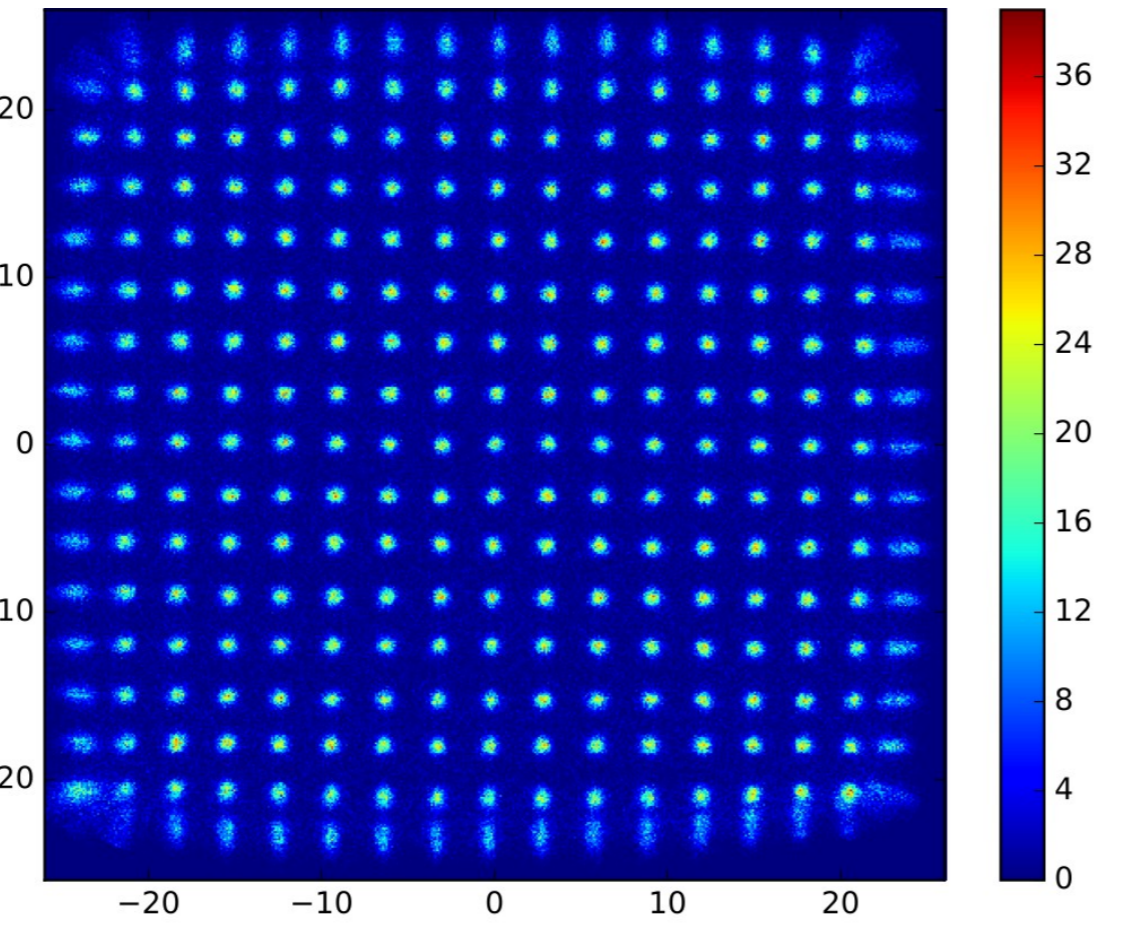
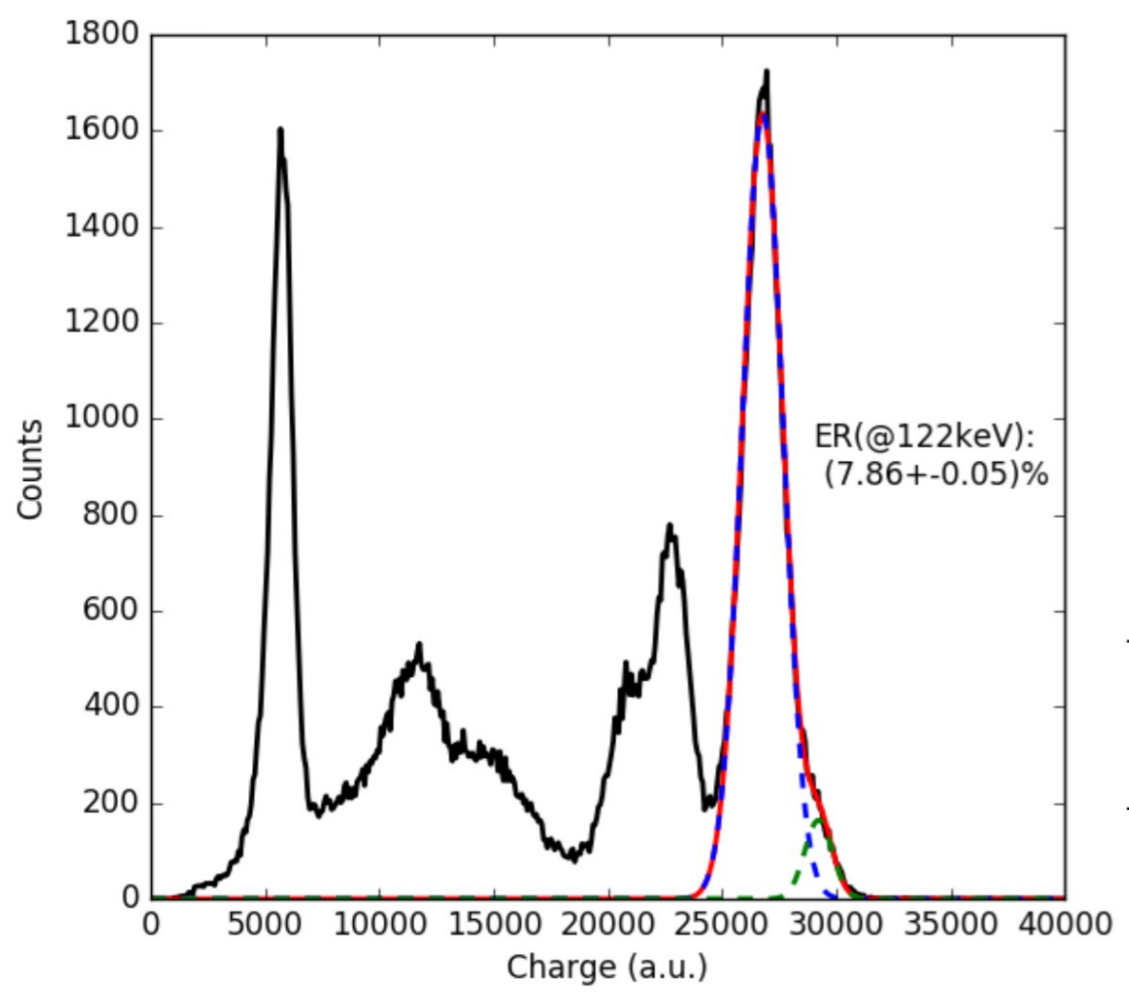
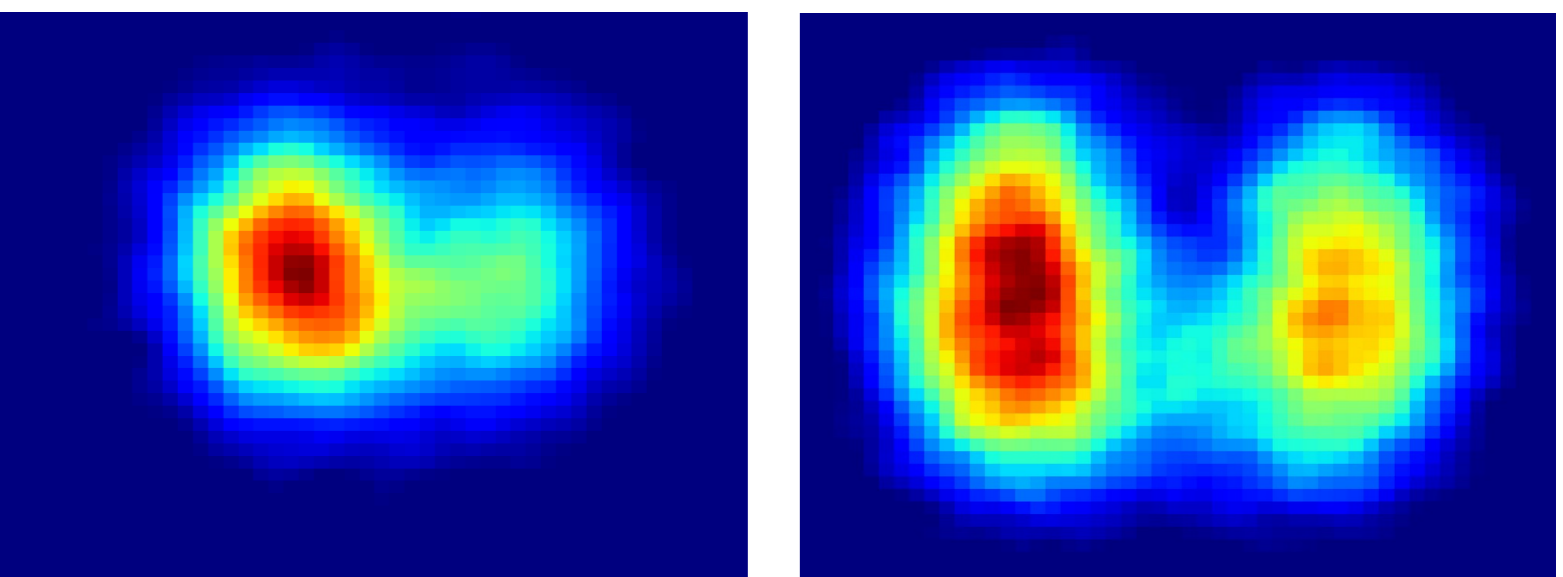


- Résolution spatiale intrinsèque submillimétrique
- Résolution énergie 7.86 % @122 keV
- Taux d'acquisition max  $13.6 \cdot 10^3 \text{ evt/s}$

**High resolution mobile gamma camera**  
@ 0.3 cm



**Gamma Camera Siemens Symbia T2 with HE collimator**  
@ 10 cm  
(SR of 13.4 mm)



Thèse Carlotta Trigila 2019

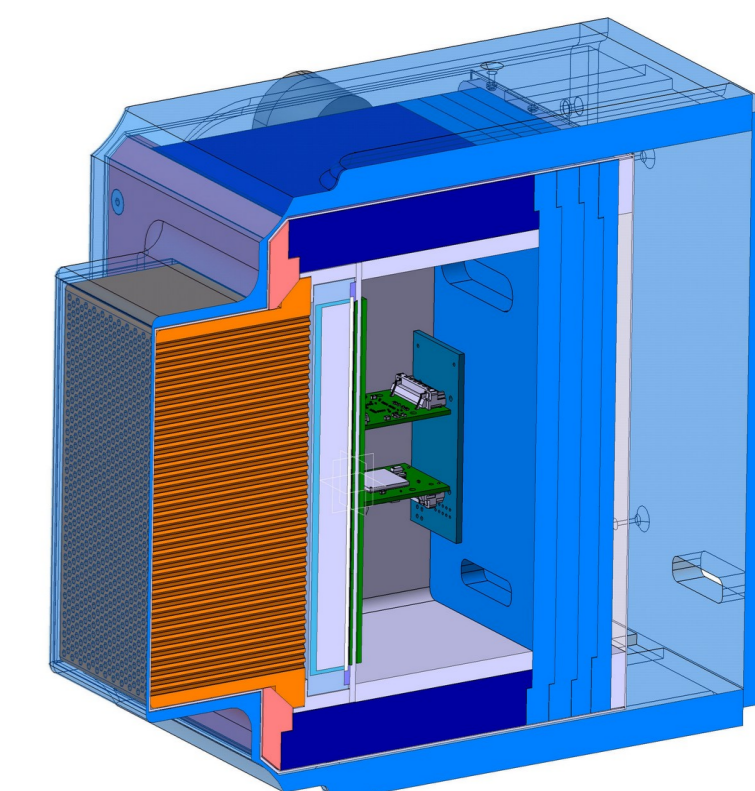
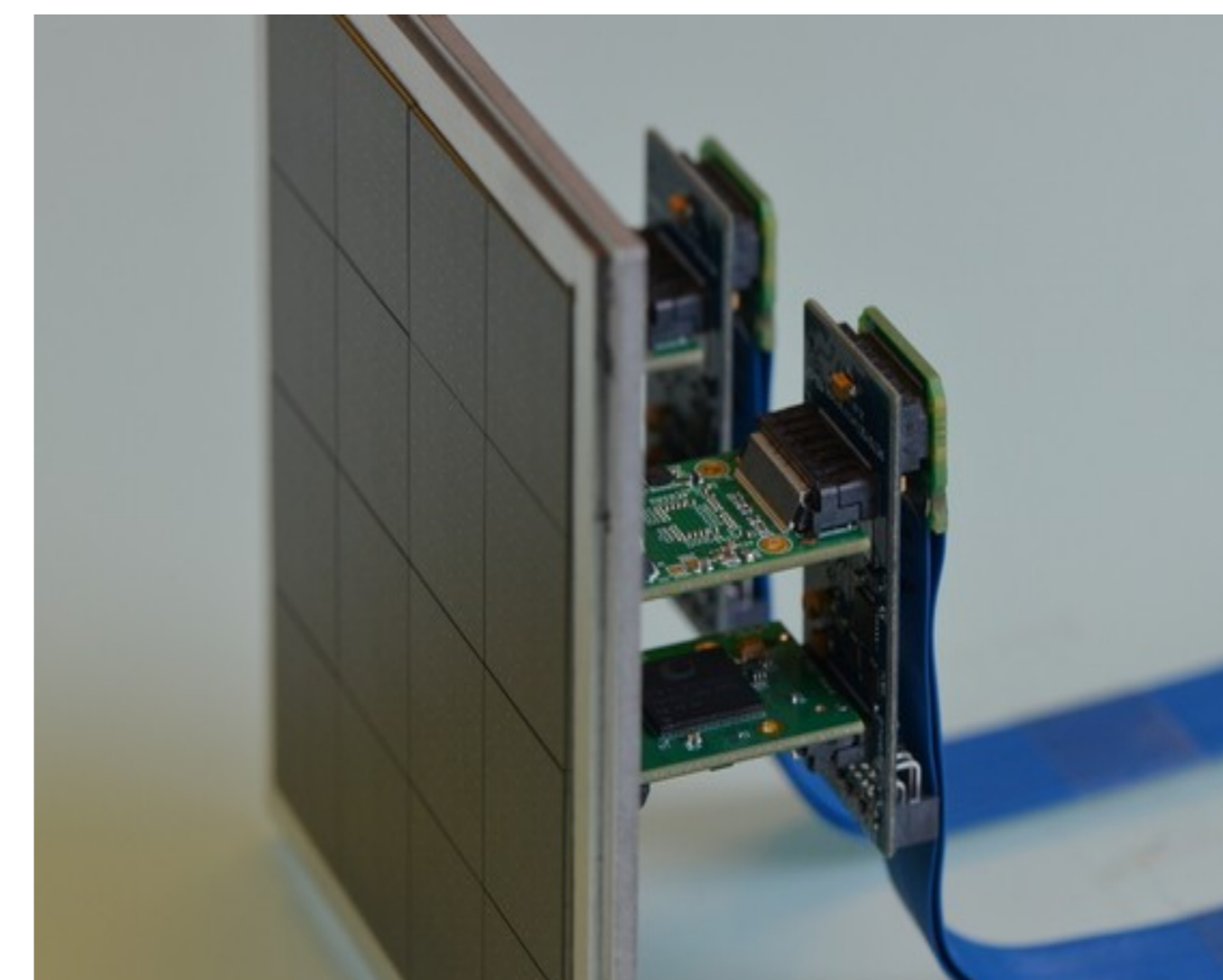
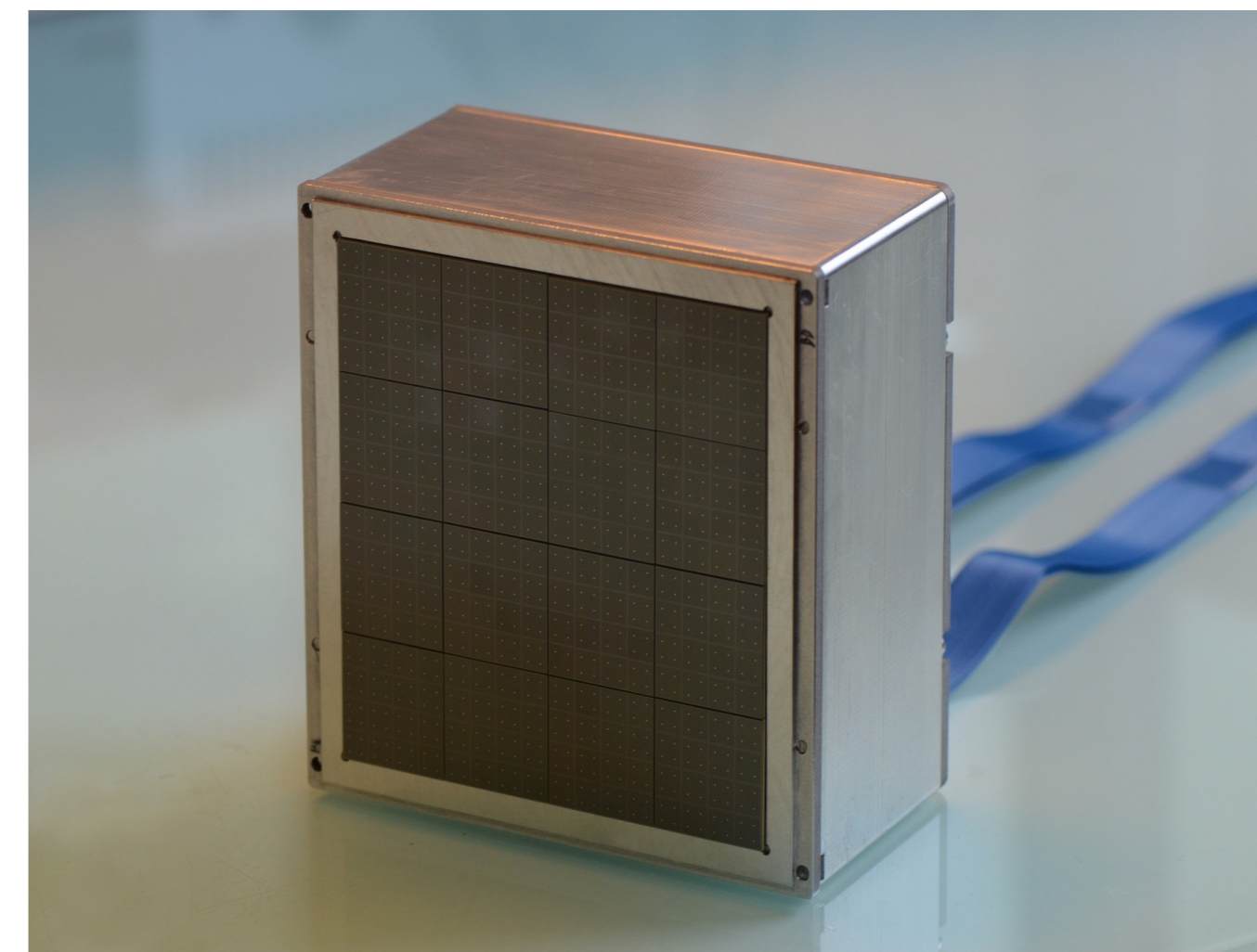


## Thèse Théo Bossis 2021-2023

### • Prototype clinique

- Champ de vue  $10 \times 10 \text{ cm}^2$
- Scintillateur  $\text{CeBr}_3$  monolithique  $10 \times 10 \times 1 \text{ cm}^3$
- Module de photodétection 256 voies MPPC  $6 \times 6 \text{ mm}^2$
- Électronique PETSys 256 voies
- Collimateur à trous parallèles tungstène par impression 3D
- Taux d'acquisition max :  $50 \cdot 10^3 \text{ evt/s}$

- Dimensions :  $18 \times 18 \times 20 \text{ cm}^3$
- Poids total : 50 kg
- Poids collimateur : 9 kg





## CONTEXT

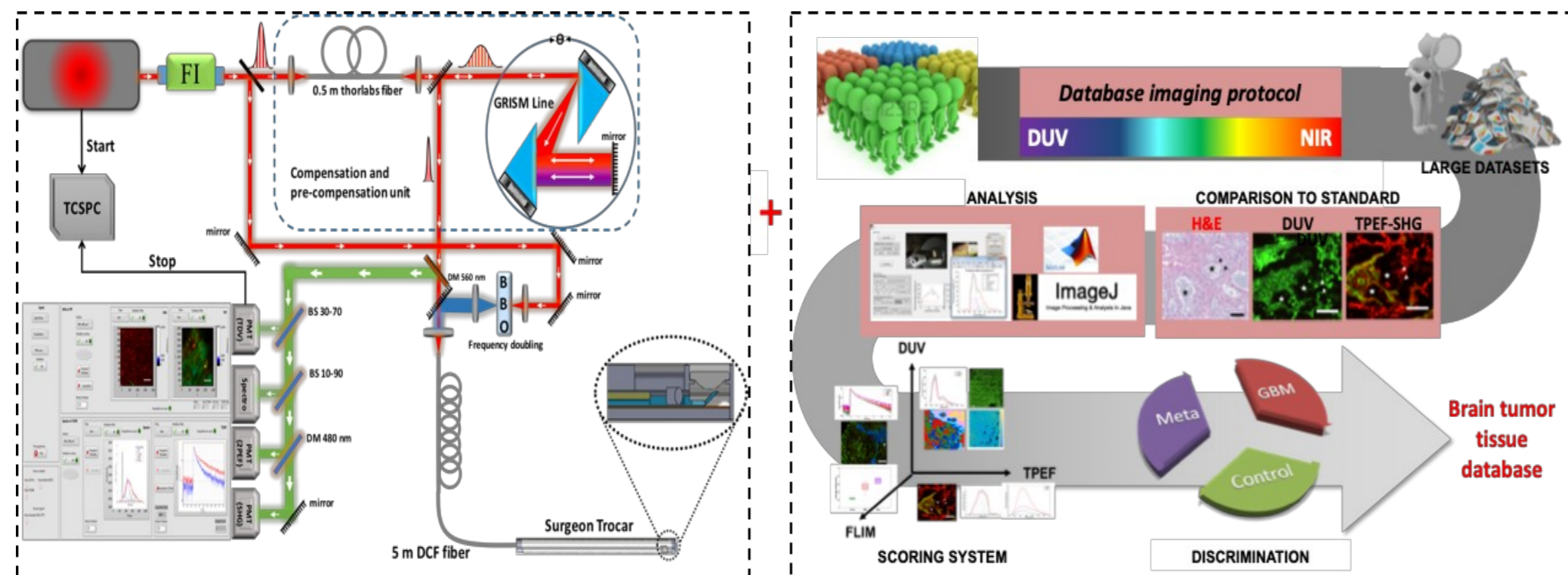
It is mandatory to perform a gross total resection of brain tumor & Minimally invasive surgery is becoming the gold standard in every surgery

**Major challenge:** The 21th neurosurgery requires new devices designed to be integrated into small surgical approaches and able to give fast and precise intraoperative tissue diagnosis, label-free, slide free and in real-time.

## SCIENTIFIC OBJECTIVES

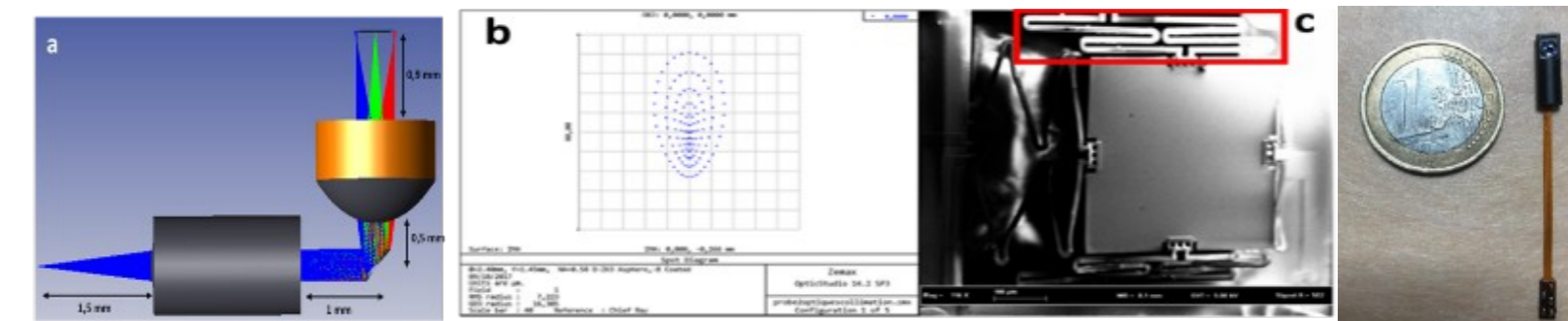
Development of a clinical multimodal non-linear endomicroscope and construction of a large optical database on different brain tissue types

## MATERIALS & METHODS

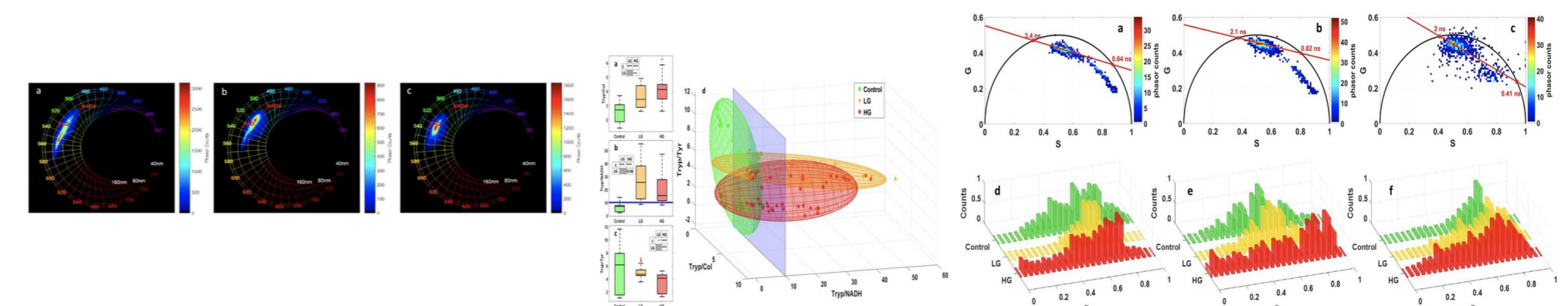


## RESULTS

- Développement d'un système de balayage miniature



- Optical Signatures Derived From Deep UV to NIR Excitation Discriminates Healthy Samples From Low and High Grades Glioma



## FINANCIAL SUPPORT

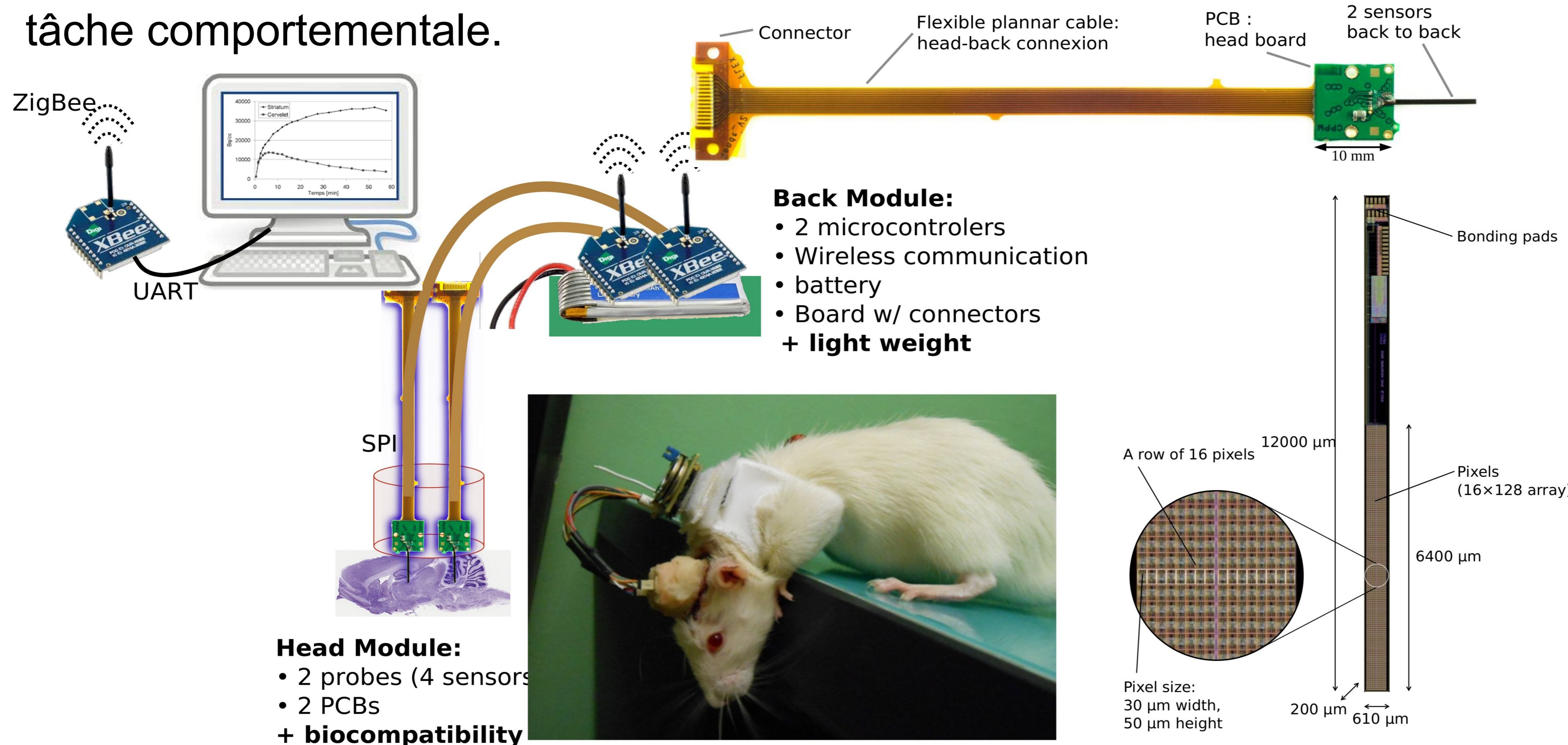
- AP Plan Cancer (projets MEMBO, MEVO, IMOP): 640 keuros
- Mission pour l'interdisciplinarité "l'instrumentation aux limites"- CNRS: 58 keuros
- Cancéropôle Île de France 65 keuros
- AP in2p3: 28 keuros
- WP3- FLI "Imagerie Interventionnelle": 30 keuros
- Contrat de prestation de service –Société NANOBACTERIE: 30 Keuros

- July 2019 clinical trial on the first prototype (PI under writing & discussion with SATT )



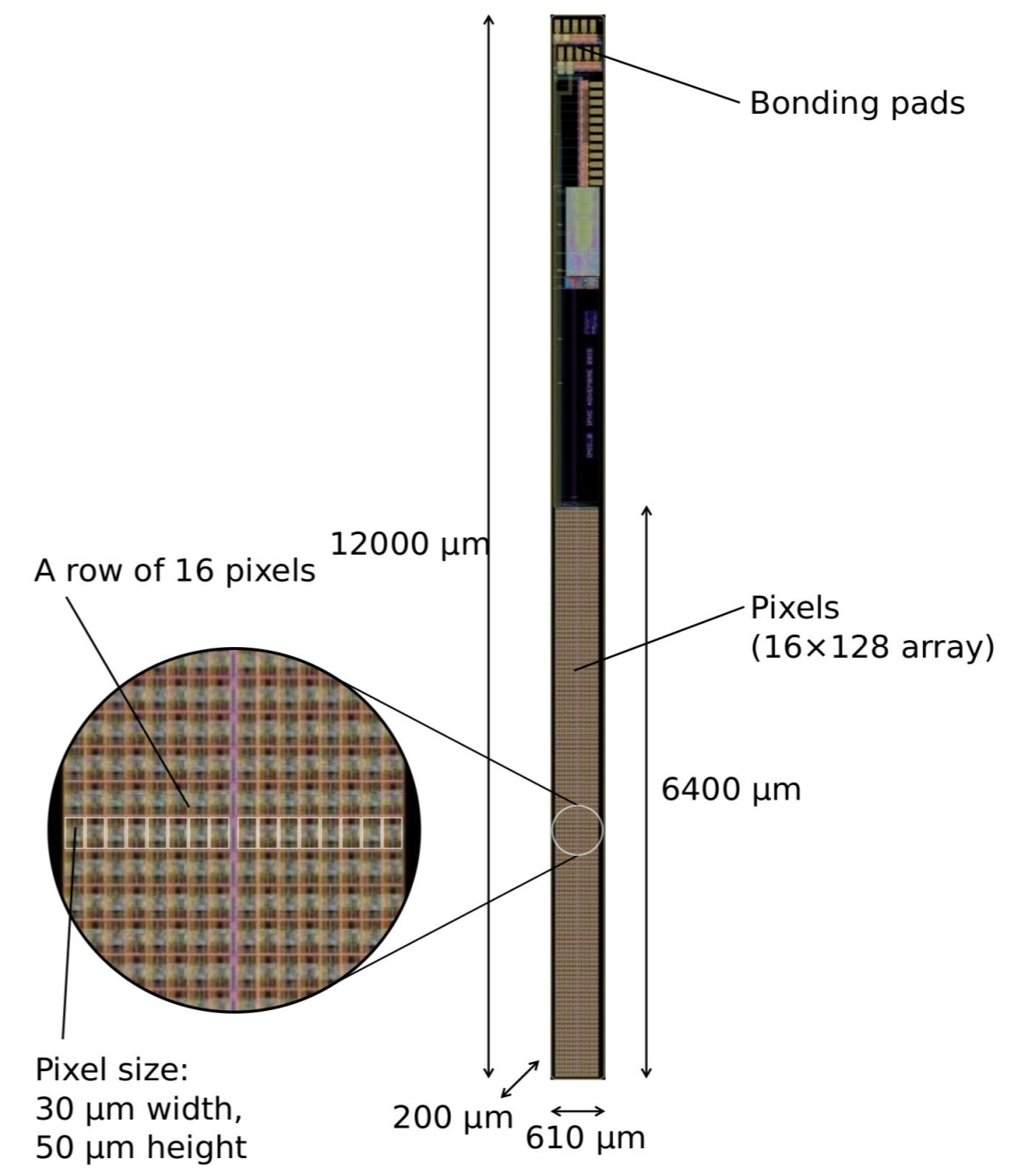
# MAPSSIC: une sonde radiosensible téléométrique pour l'imagerie comportementale

- Complémentaire à l'imagerie TEP : microimplants téléométriques radiosensibles aux  $\beta^+$  laissant l'animal éveillé et libre de ses mouvements et permettant la mesure d'un radiotracer lors d'une tâche comportementale.



- 1<sup>er</sup> prototype : 2 capteur MAPS montés sur un unique PCB
- Simulations MC pour la validation physique dans une géométrie de cerveau et sur fantômes d'eau.

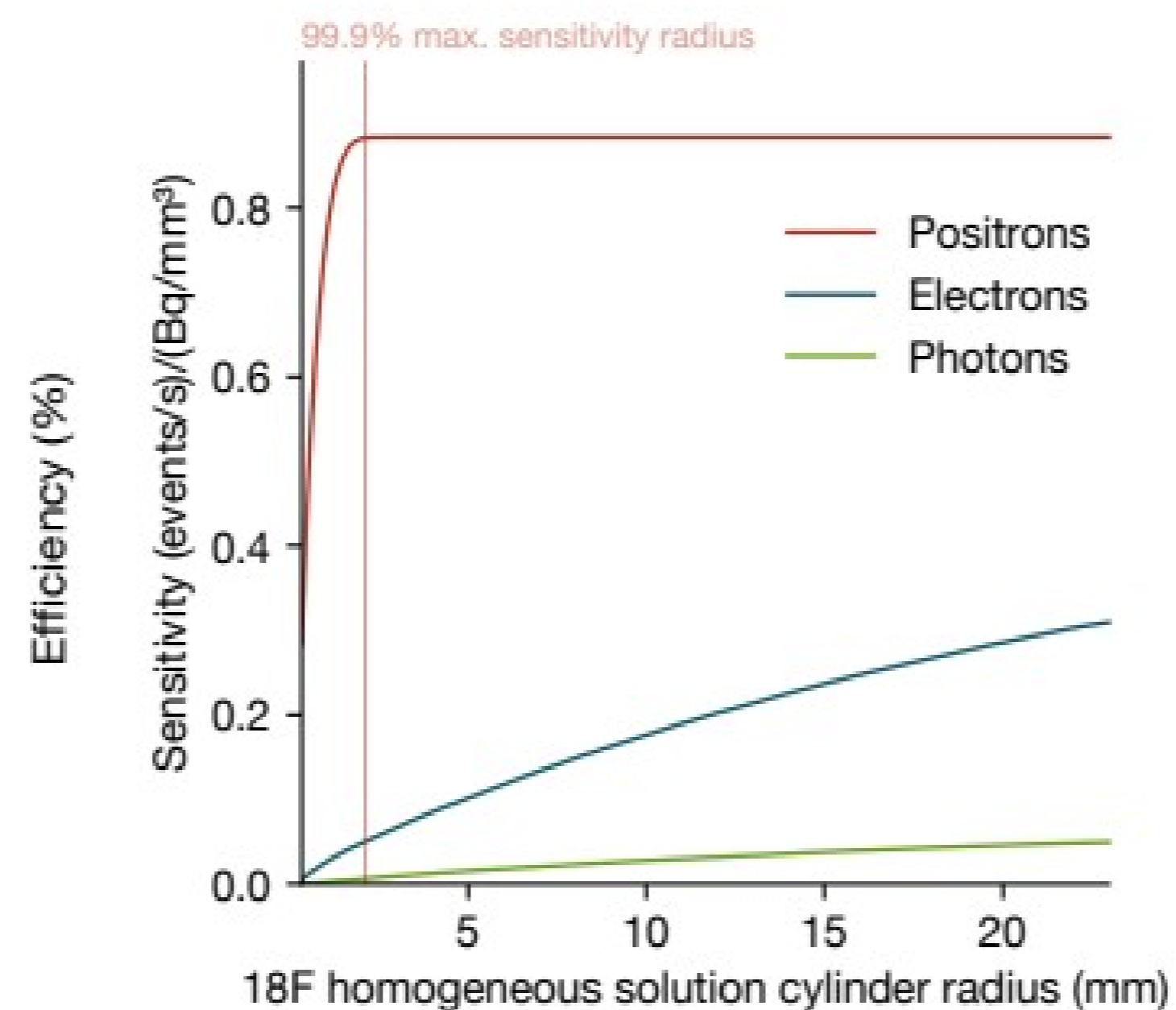
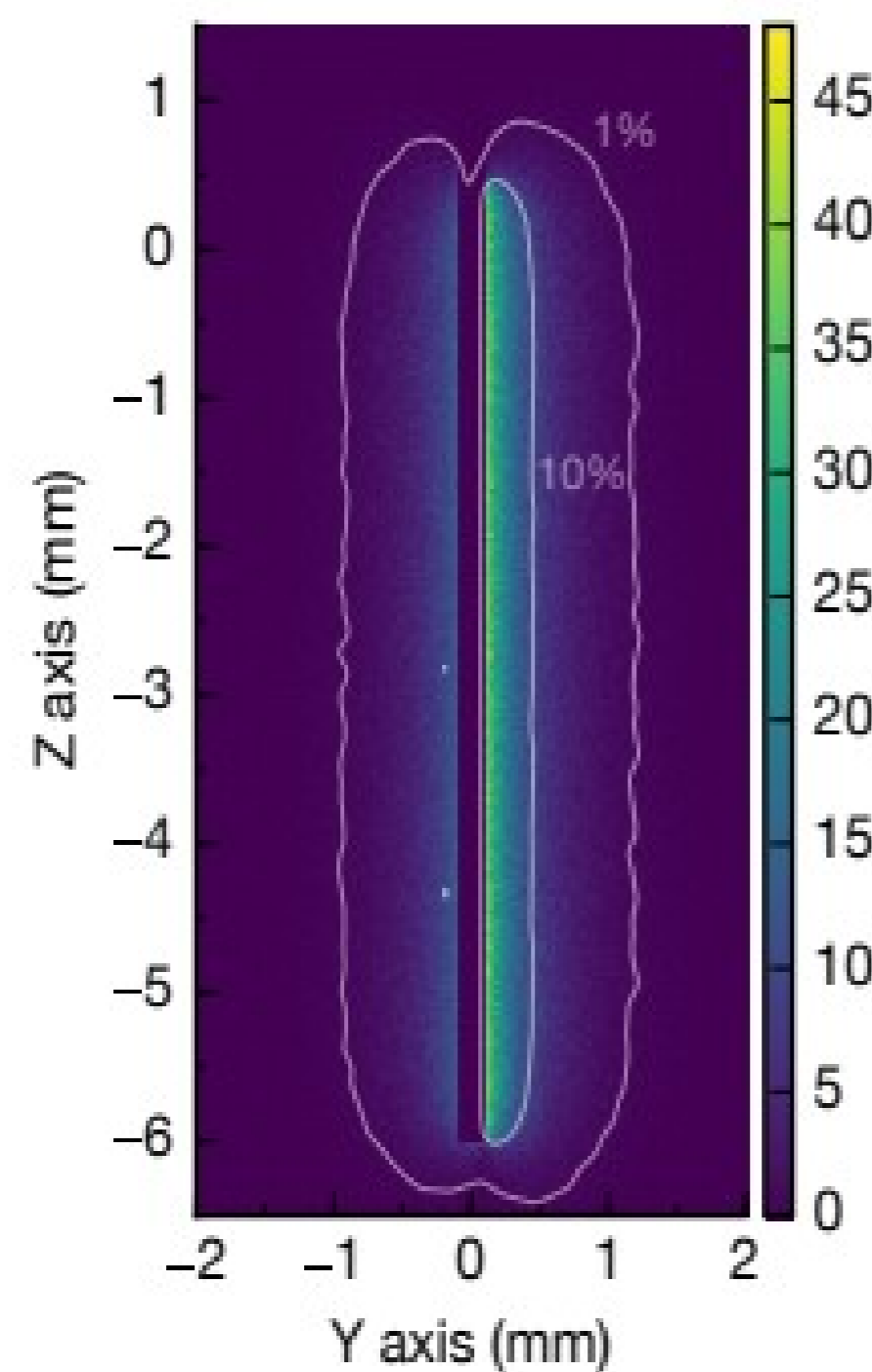
• **Thèse Luis Ammour (2018)**



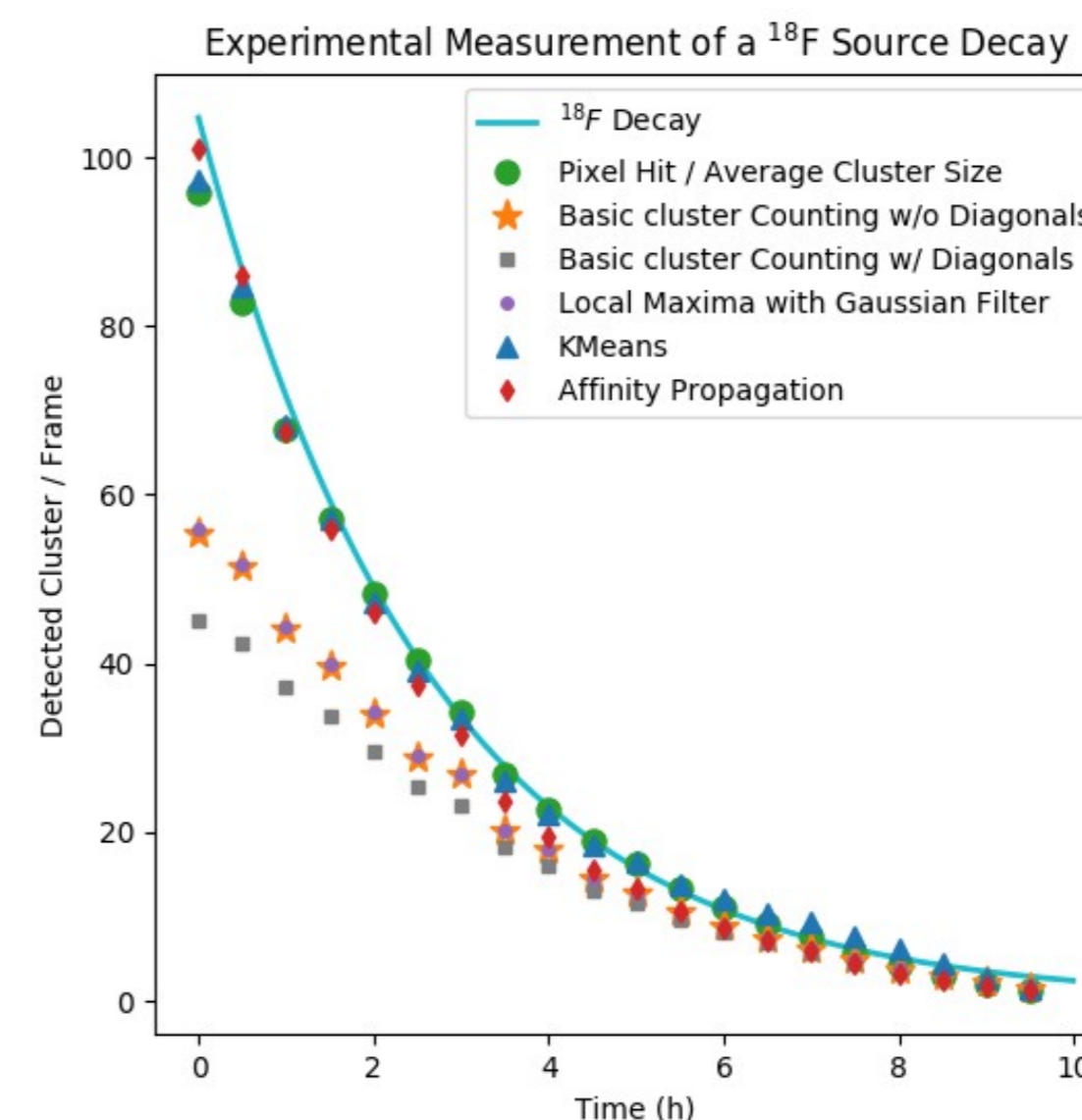


- Courte portée des  $\beta^+$  permet la mesure de la concentration locale de radiotraceurs (simulation MC)
- Comptage d'événements par clustering des images

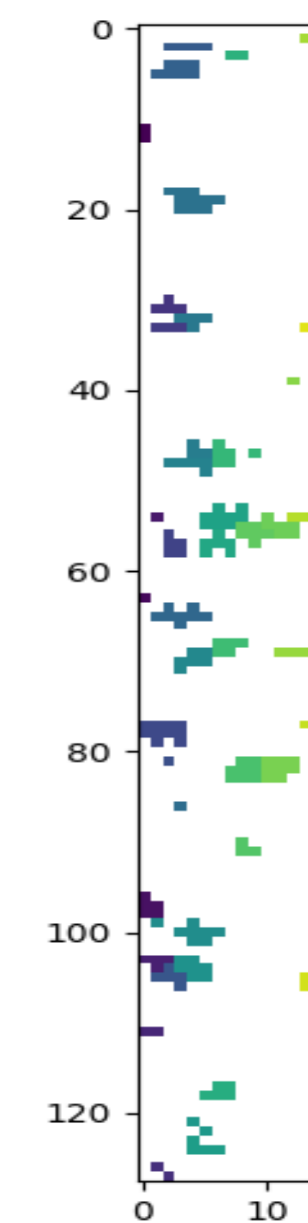
- 2<sup>nd</sup> prototype actuellement en fabrication
- Nouvelle électronique de sac-à-dos
- Connectique carte-tête
- Thèse Samir El Ketara (démarre 2022)



Haute sensibilité aux  $\beta^+$



Correction de la linéarité  
du taux de comptage





# CREATIS Research Lab



## Cancer center

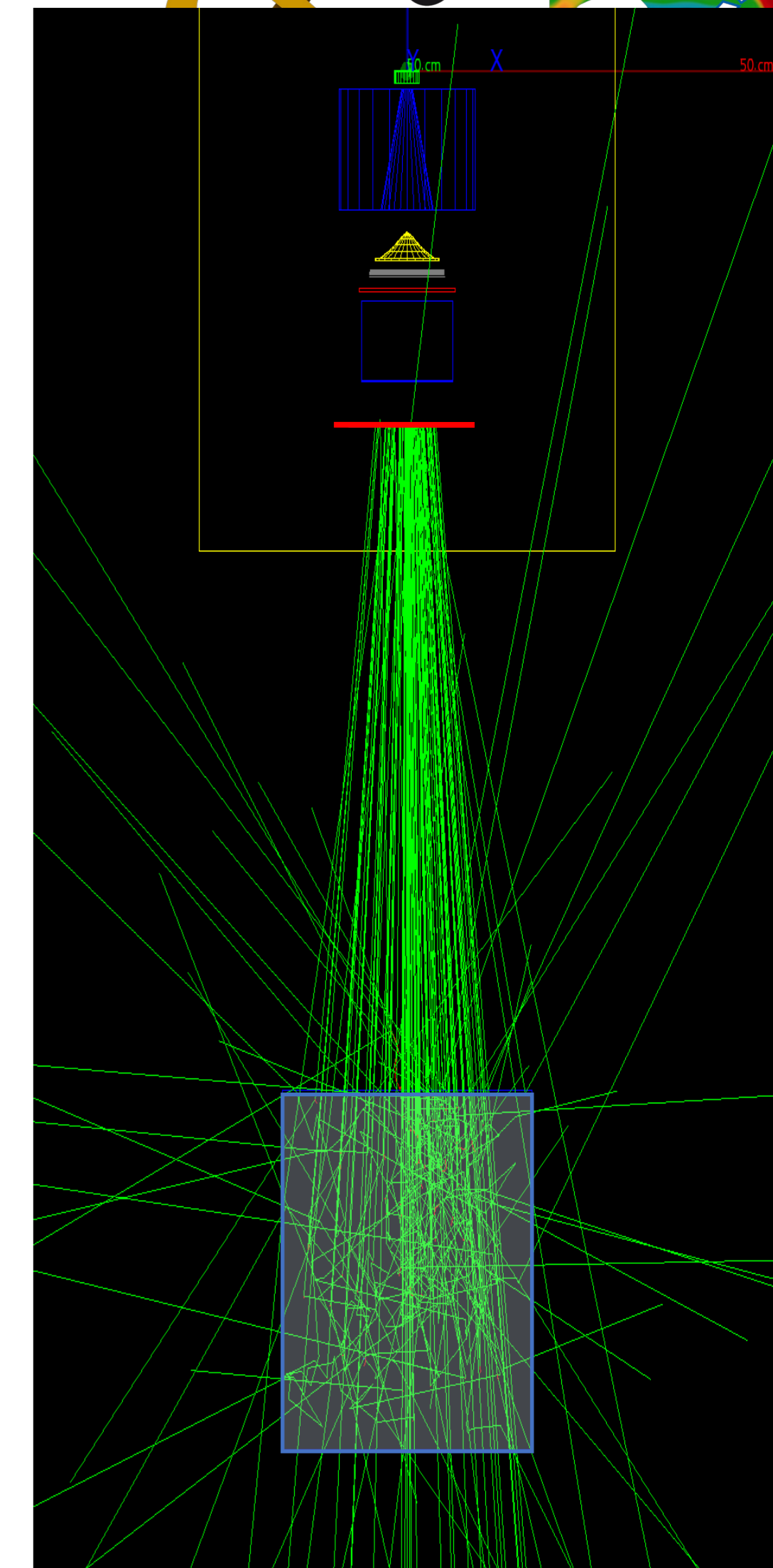
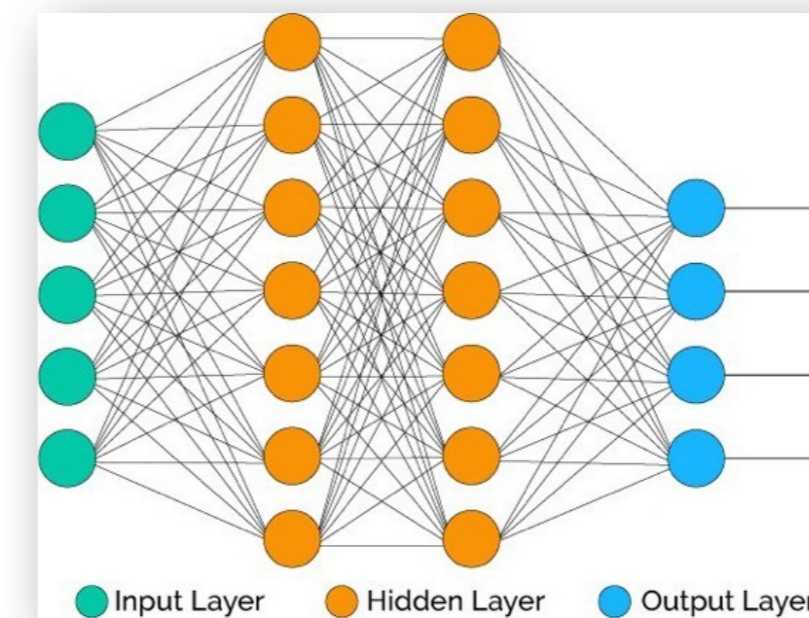


- Image reconstruction
- Monte Carlo simulations
- EBRT and Nuclear Medicine



# Activities 1/2

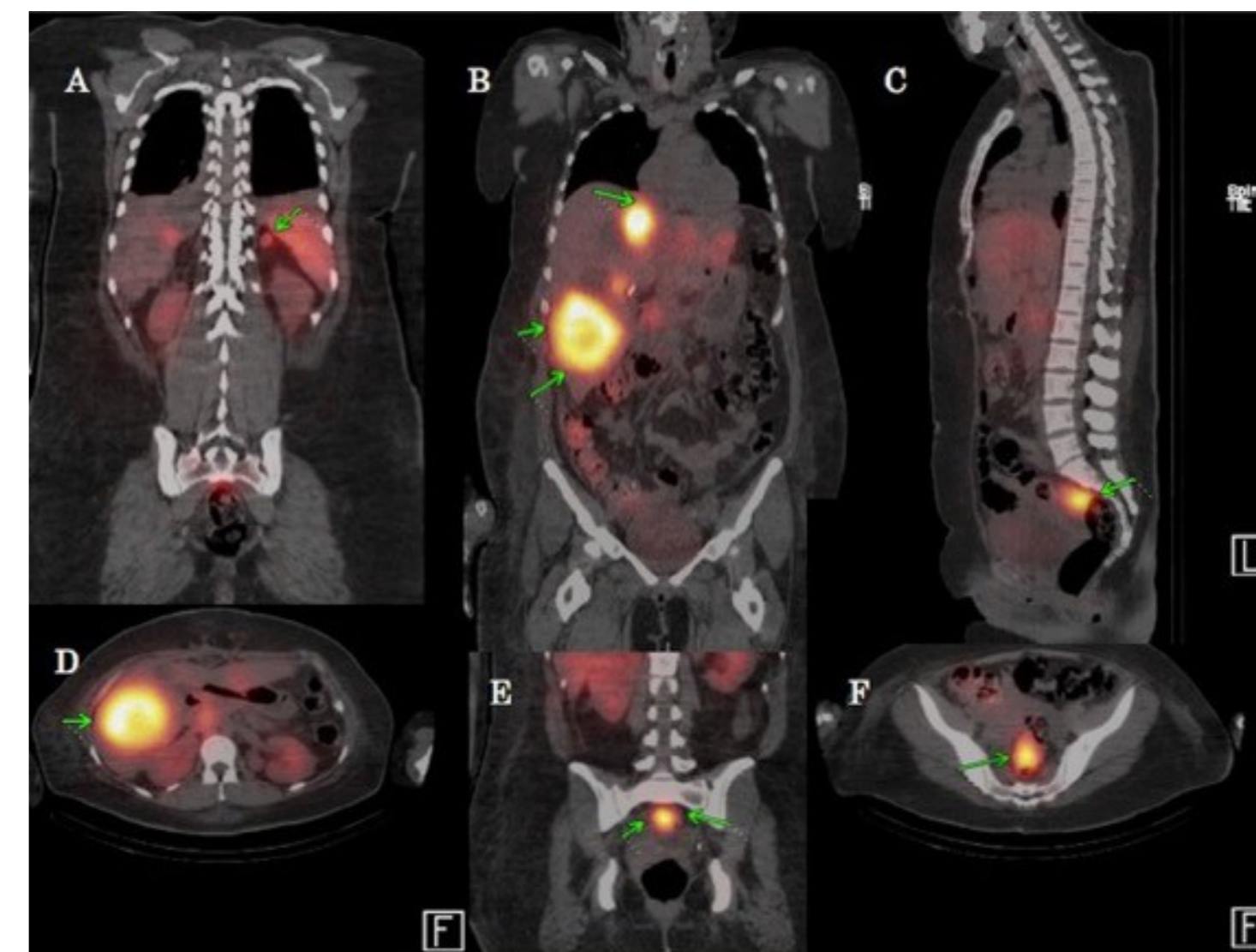
- Monte Carlo simulations
  - **Imaging**: SPECT, PET, Compton Camera, protonCT, CBCT, etc  
[Salvadori2020, Etxebeste2020, Winterhalter2020, Labour2021, Elia2020 ...]
  - **Dosimetry**: radionuclide therapy
  - OpenGate collaboration [Sarrut2014, Sarrut2021]
- AI for MC simulations
  - Deep Learning for detector modeling
  - GAN for phase-space modeling
  - [Sarrut2018, Sarrut2019, Sarrut2021]





# Activities 2/2

- Radionuclide therapy dosimetry
  - Lu-177 for NETs and PSMA
  - Y-90 SIRT (liver)
  - Patients from Léon Bérard cancer center
  - Collaboration: Philips, Siemens
  - New Veriton CZT SPECT system
- 4D SPECT reconstruction
  - RTK toolkit
  - Collaboration: Kitware
- Compton Camera
  - For nuclear medicine
  - Collaboration: IP2I, LPSC

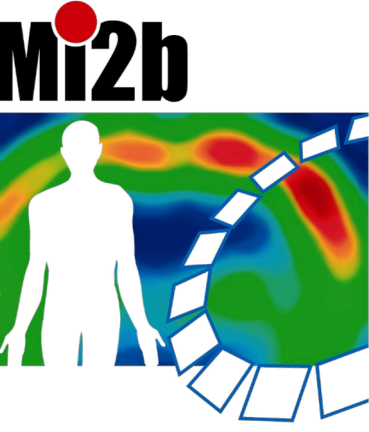


New Veriton-CT SPECT system



# CREATIS

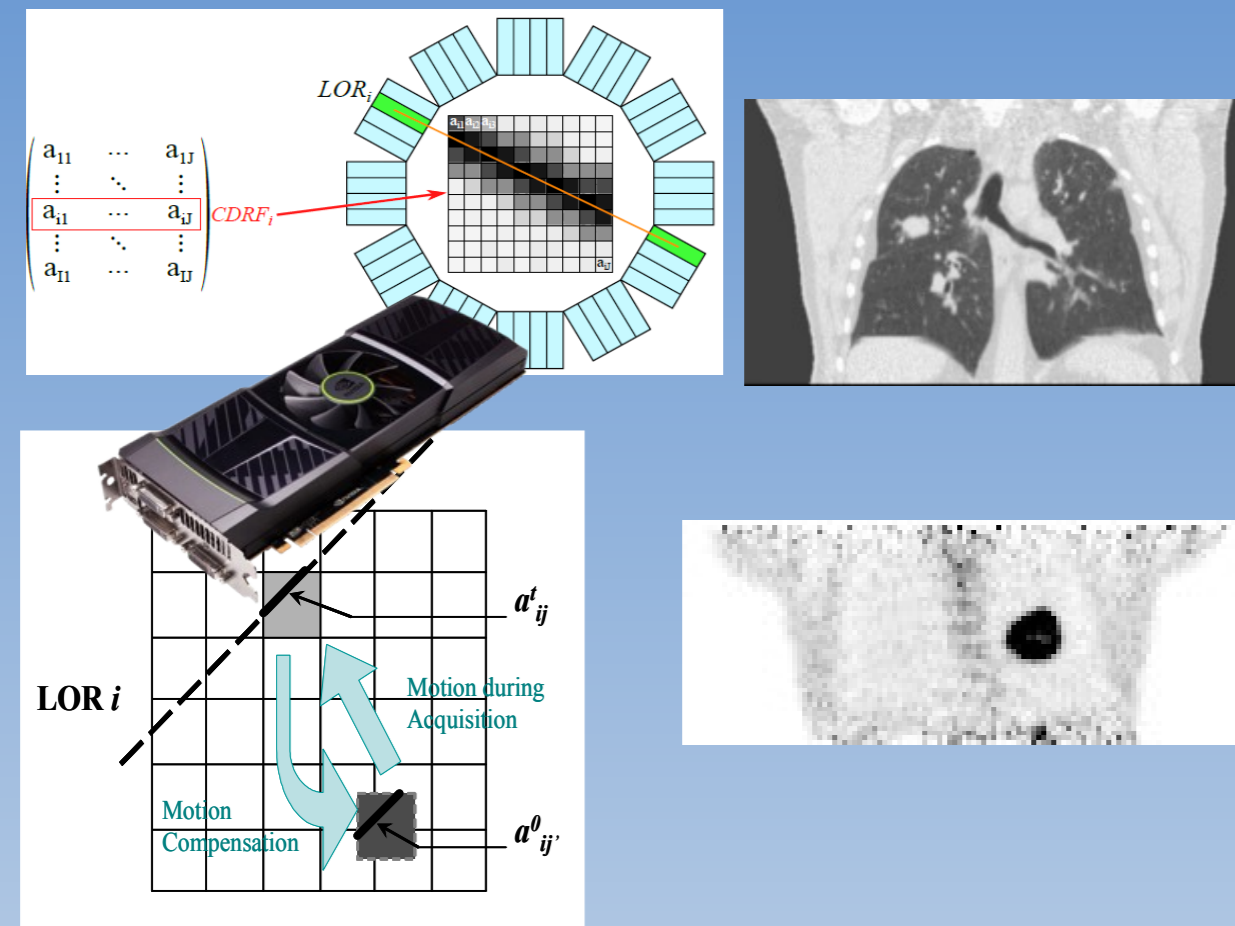
  
Lyon, France  
Depuis 80 ans, nos connaissances  
battent de nouveaux mondes



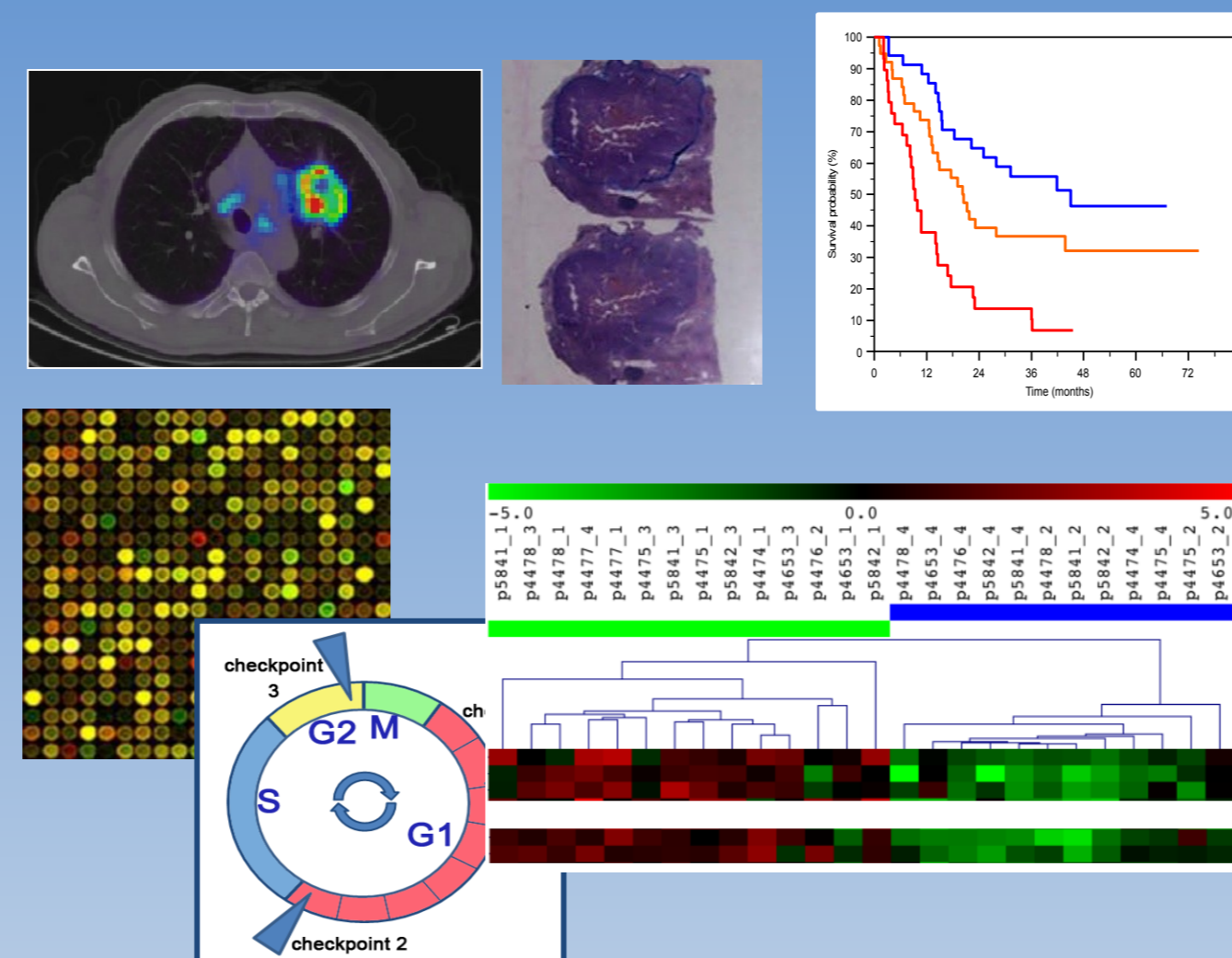


## Therapy Action guided by Multimodality Imaging in Oncology

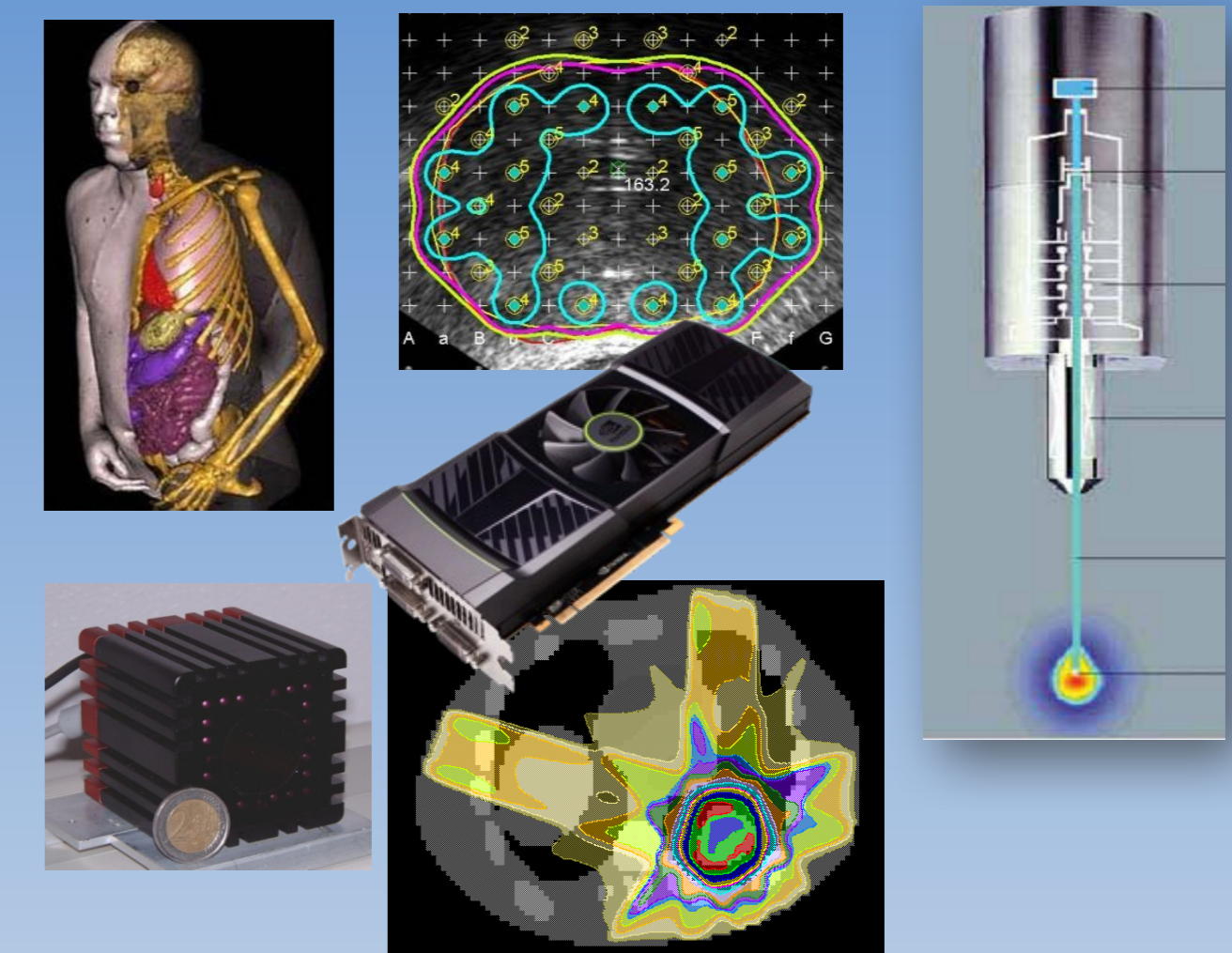
### Axe 1: Multi-dimensional tomographic image reconstruction



### Axe 2: Multi-parametric modeling for therapy optimisation



### Axe 3: Image guided radiotherapy and dosimetry

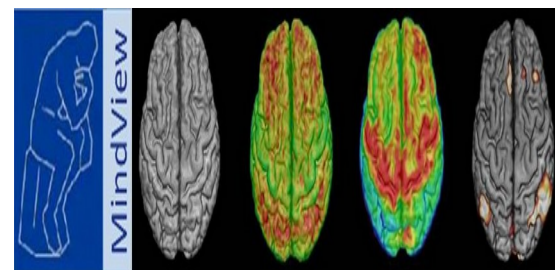




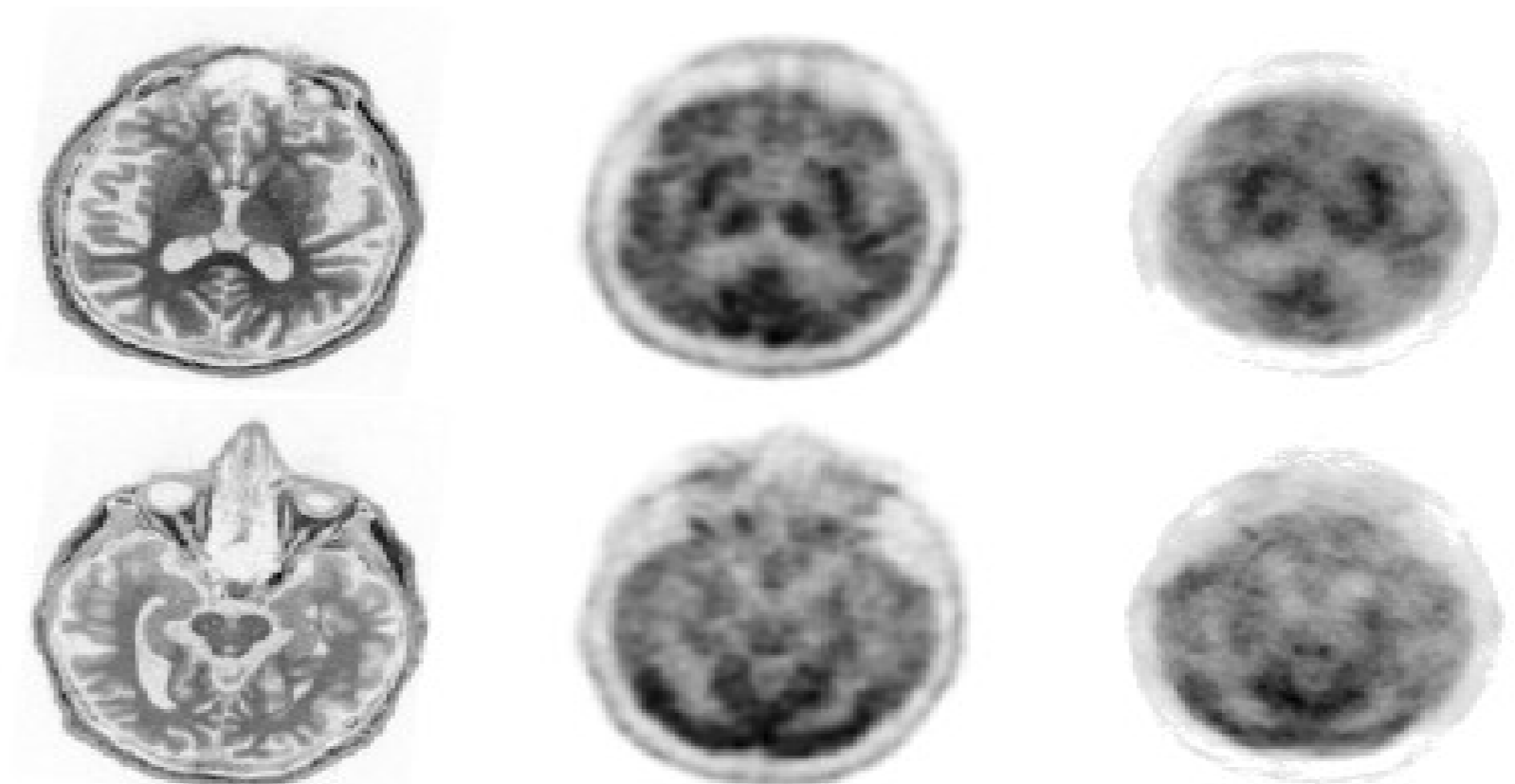
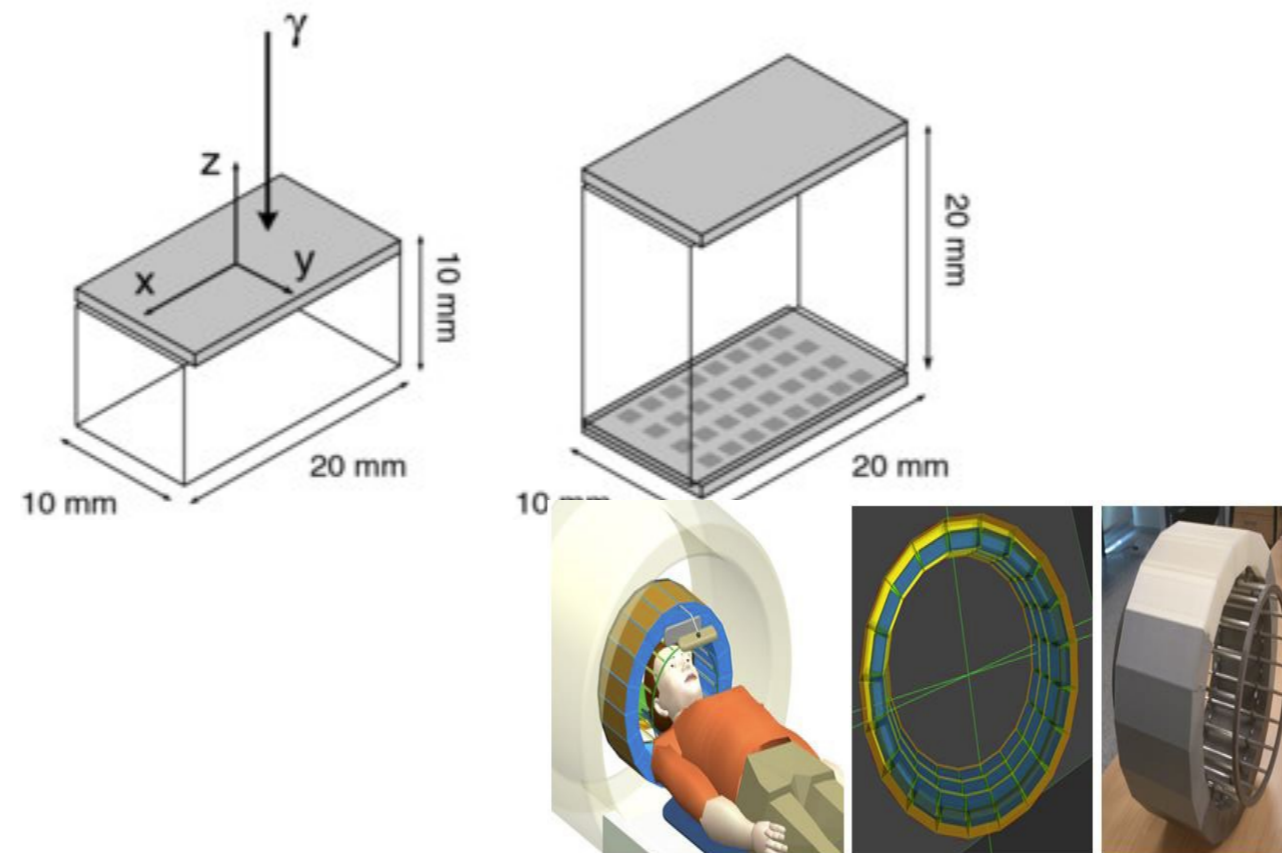
# Multi-dimensional Image Reconstruction: detector level



- ✓ Use of deep learning for the determination of interactions within monolithic crystals for high resolution PET imaging



collaboration: Oncovision Valencia, INFN Rome, sensL, TUM Munich, Karolinska Stockholm

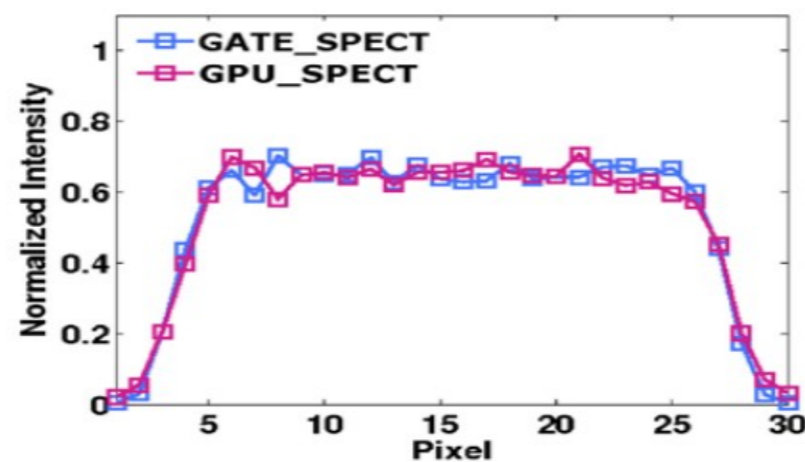
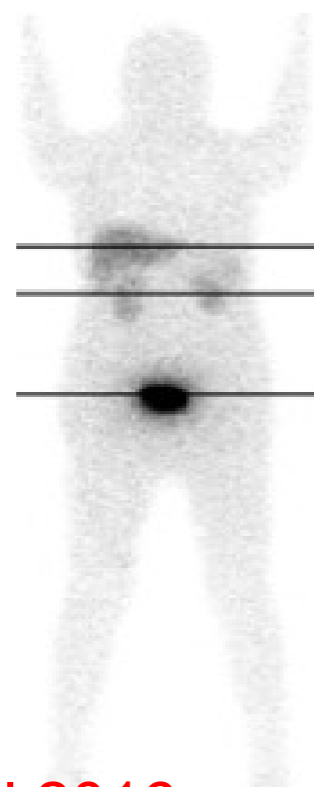
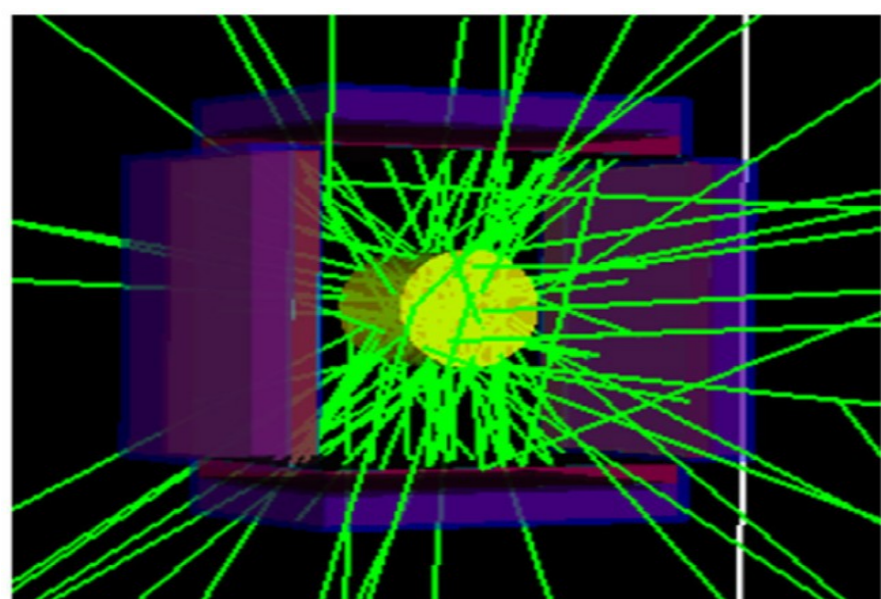


Iborra, Phys Med Biol 2019



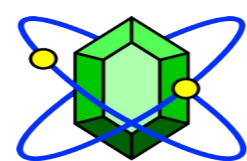
- ✓ Fast Monte Carlo Simulation based SPECT system

Axis 3



Steps	Activity (GBq)	fmcGATE 1 CPU core	fmcGGEMS GTX 690	fmcGGEMS GTX 980	fmcGGEMS GTX 980 ti
1	7.56	17 days	25h	18h	12h
2	7.58	17 days	26h	20h	13h
3	7.59	18 days	28h	20h	13h
4	7.61	17 days	25h	18h	12h
5	7.62	17 days	25h	18h	12h
<b>Total</b>	<b>37.96</b>	<b>86 days</b>	<b>5 days 9h</b>	<b>4 days</b>	<b>2 days 14h</b>
<b>Acceleration</b>	-	-	<b>16</b>	<b>22</b>	<b>33</b>

Garcia, Phys Med Biol 2016

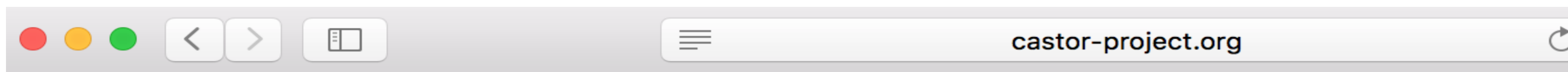




# Unique Multi-dimensional image reconstruction platform



Depuis 80 ans, nos connaissances  
bâtissent de nouveaux mondes



CASToR

Registration

Documentation

Benchmarks

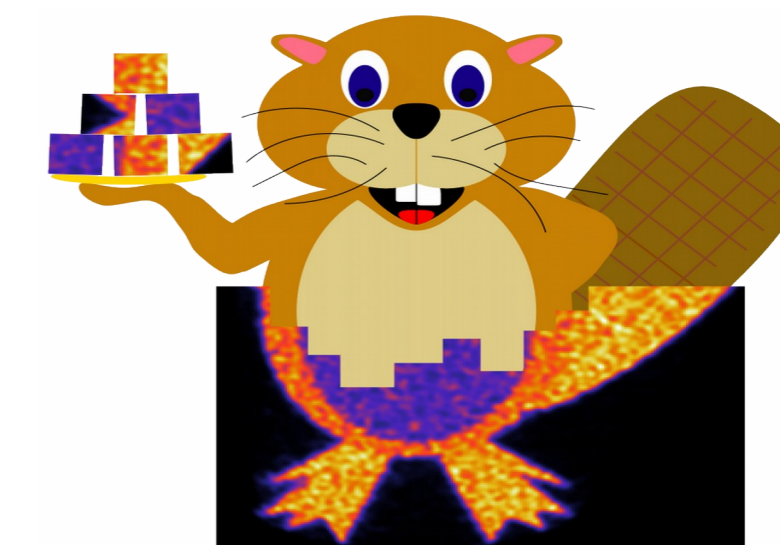
Data converters

Mailing-List

Organization

## CASToR - Customizable and Advanced Software for Tomographic Reconstruction

CASToR is an open-source multi-platform project for 4D emission (PET and SPECT) and transmission (CT) tomographic reconstruction. This platform is a scalable software providing both basic image reconstruction features for "standard" users and advanced tools for specialists in the reconstruction field, to develop, incorporate and assess their own methodologies in image reconstruction (such as specific projectors, optimization algorithms, dynamic data modeling, etc) through the implementation of new classes.



- ✓ 1st public release: May 2017
- ✓ 500 registered users

Merlin, Phys Med Biol 2018



## Functional volume segmentation

### MEDICAL PHYSICS

The International Journal of Medical Physics Research and Practice

Task Group Report | [Free Access](#)

#### Classification and evaluation strategies of auto-segmentation approaches for PET: Report of AAPM task group No. 211

Mathieu Hatt, John A. Lee, Charles R. Schmidtlein, Issam El Naqa, Curtis Caldwell ... [See all authors](#)

First published: 24 January 2017 | <https://doi.org/10.1002/mp.12124> | Citations: 67

2 licences



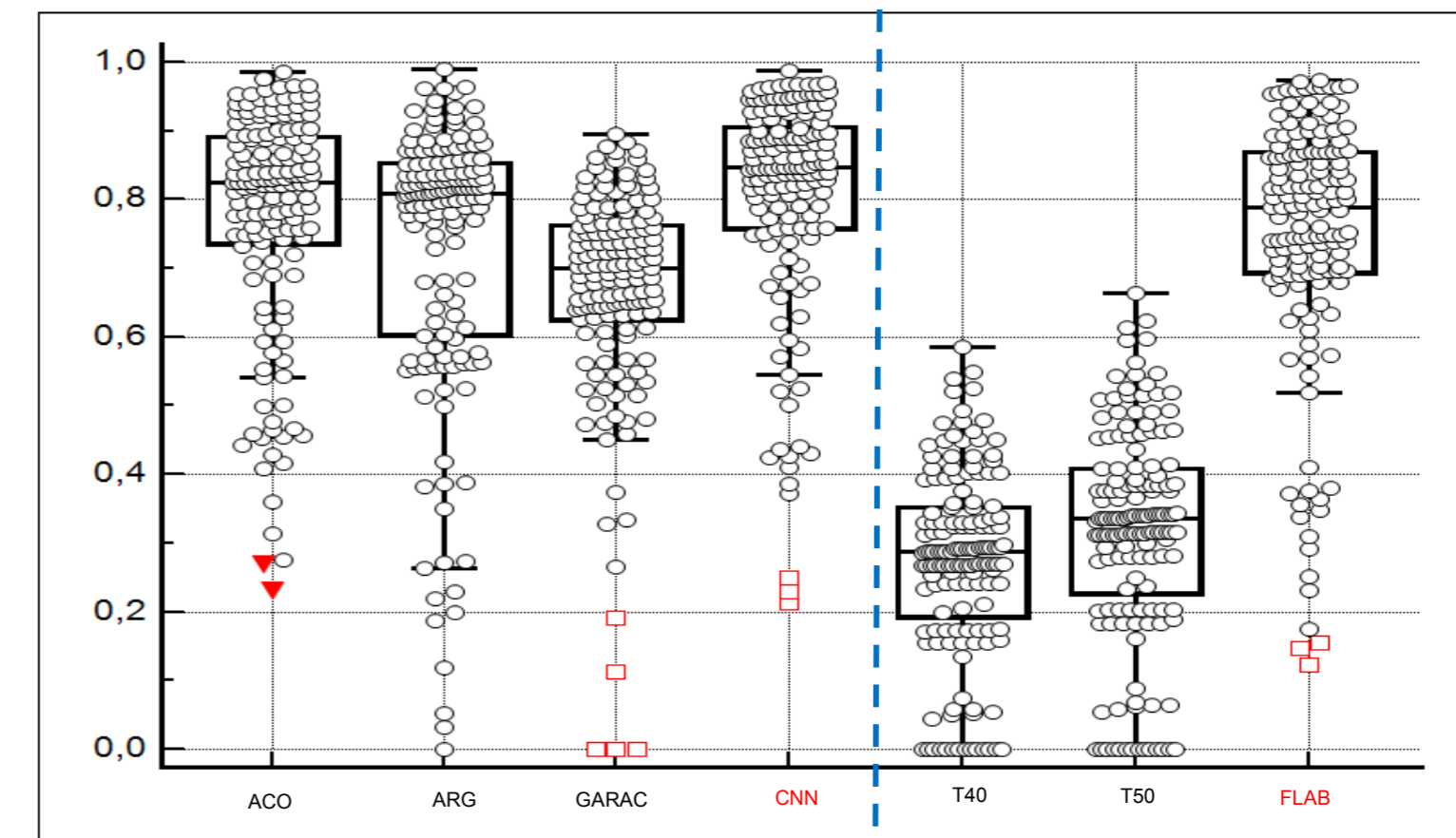
Medical Image Analysis  
Volume 44, February 2018, Pages 177-195



#### The first MICCAI challenge on PET tumor segmentation

HCERES

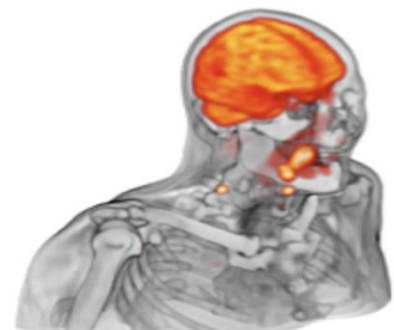
Mathieu Hatt<sup>a</sup>, Baptiste Laurent<sup>a</sup>, Anouar Ouahabi<sup>a</sup>, Hadi Fayad<sup>a</sup>, Shan Tan<sup>b</sup>, Laquan Li<sup>b</sup>, Wei Lu<sup>c</sup>, Vincent Jaouen<sup>a</sup>, Clovis Tauber<sup>d</sup>, Jakub Czakon<sup>e</sup>, Filip Drapejkowski<sup>e</sup>, Witold Dyrka<sup>e,f</sup>, Sorina Camarasu-Pop<sup>g</sup>, Frédéric Cervenkansky<sup>g</sup>, Pascal Girard<sup>g</sup>, Tristan Glatard<sup>h</sup>, Michael Kain<sup>i</sup>, Yao Yao<sup>i</sup> ... Dimitris Visvikis<sup>a</sup>



Hatt, Med Im Anal 2018

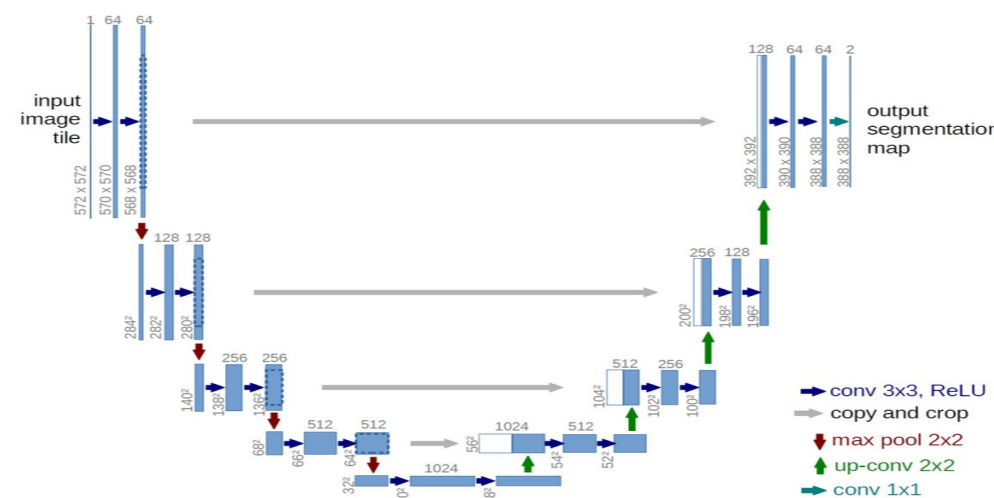
#### HECKTOR

Head and neck TumOR segmentation



Sponsored by Siemens Healthineers Switzerland

1<sup>st</sup> out of more than 20



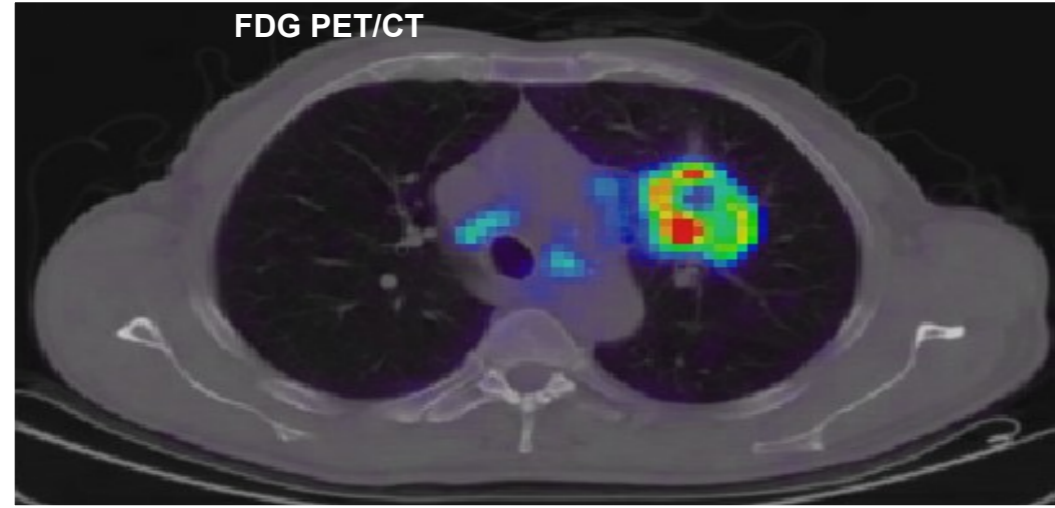
Iatsen, Eur J Nucl Med 2021



4<sup>th</sup> out of more than 120

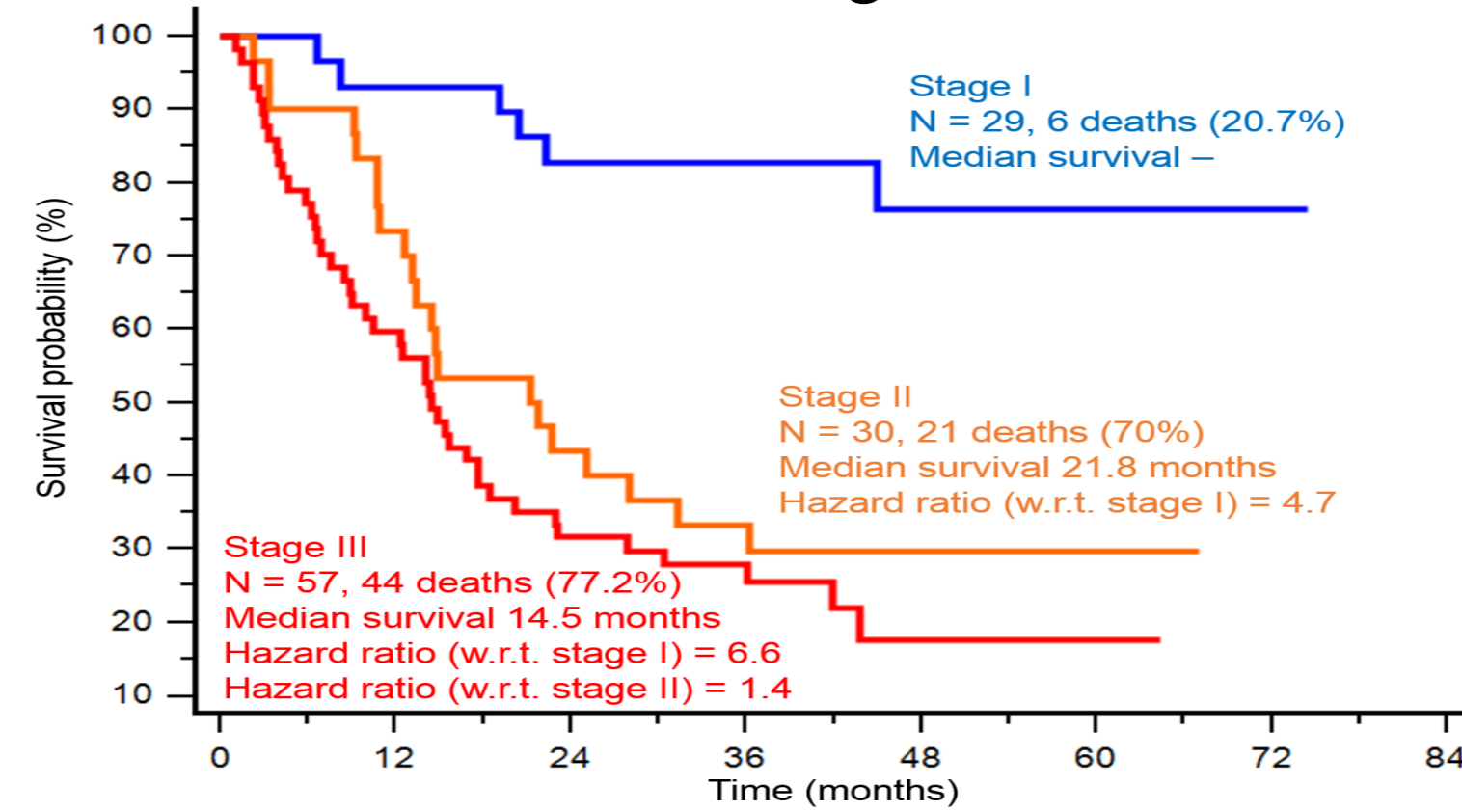


## Lung

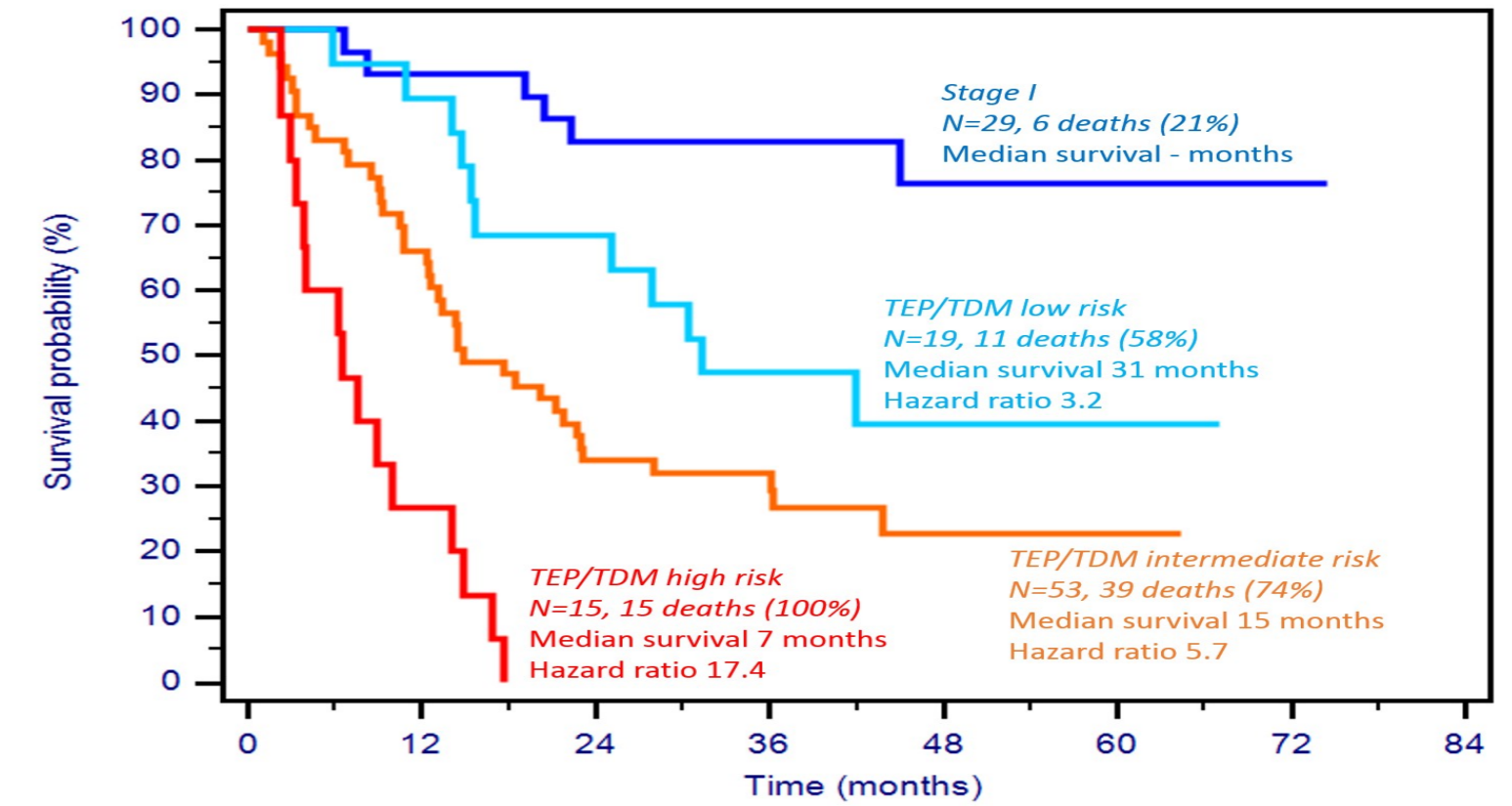


8 publications

## Stage



## Stage, PET vol, PET & CT entropy



Desseroit, Eur J Nucl Med 2016

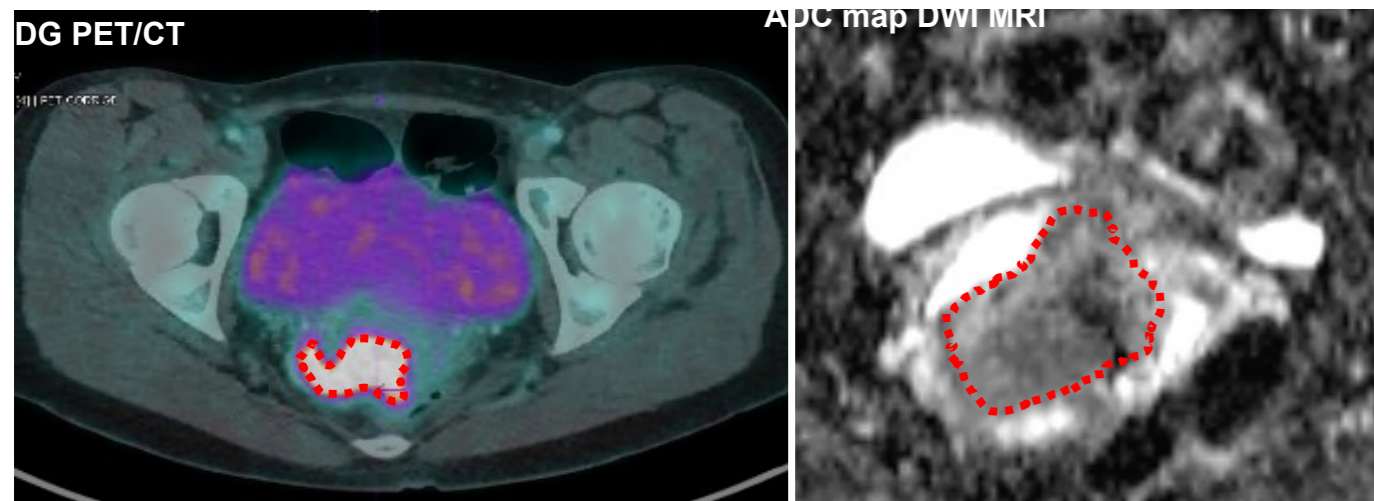
## PRTK PRINCE: prospective study (>250 patients included)



DIRECTION GÉNÉRALE DE L'OFFRE DE SOINS

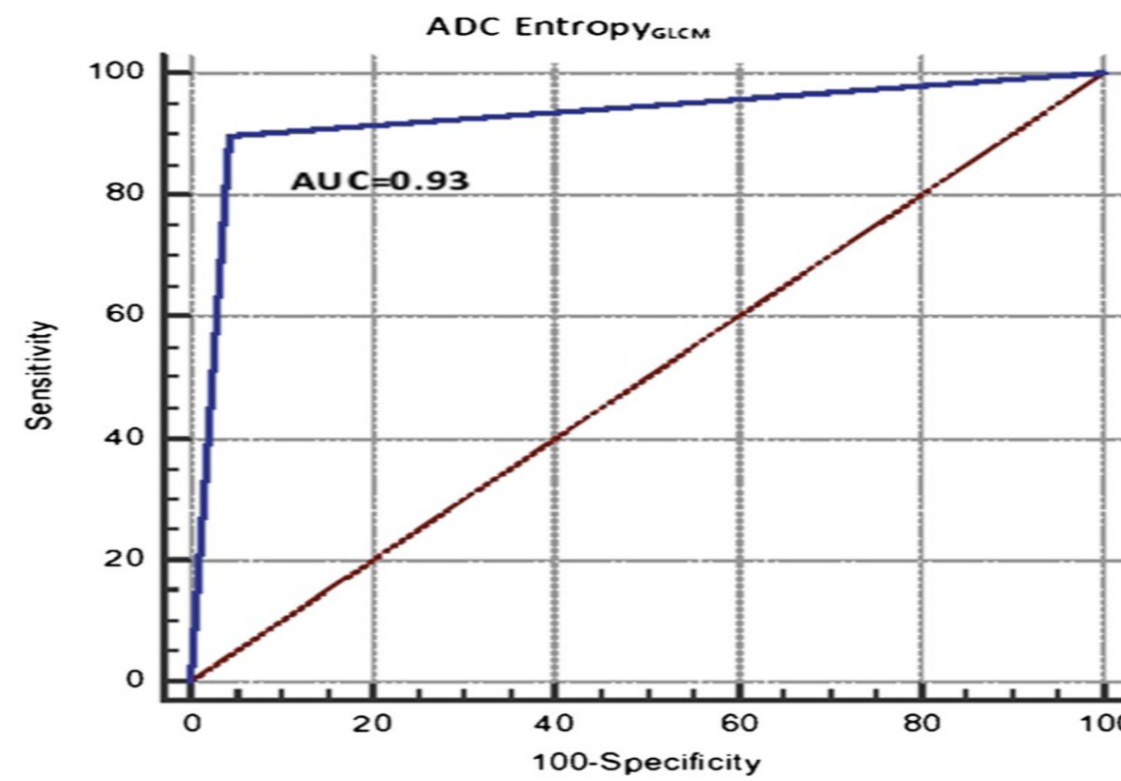


## Cervical

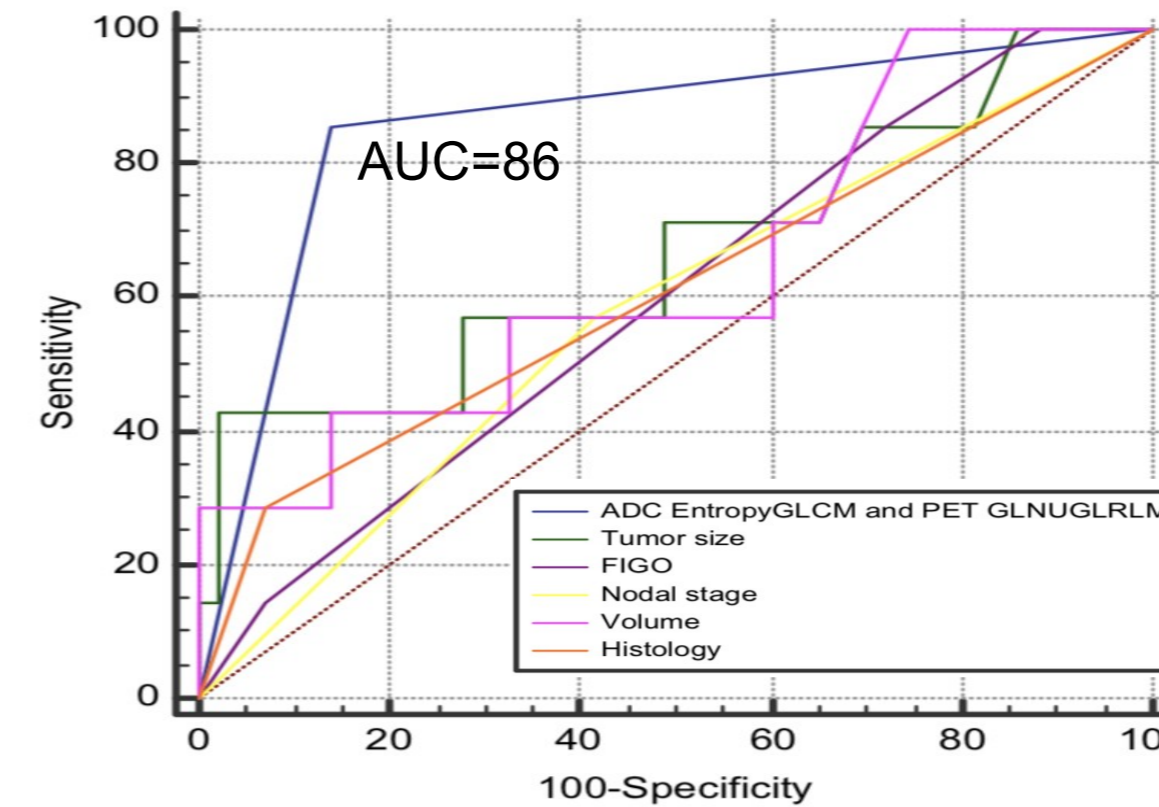


3 publications

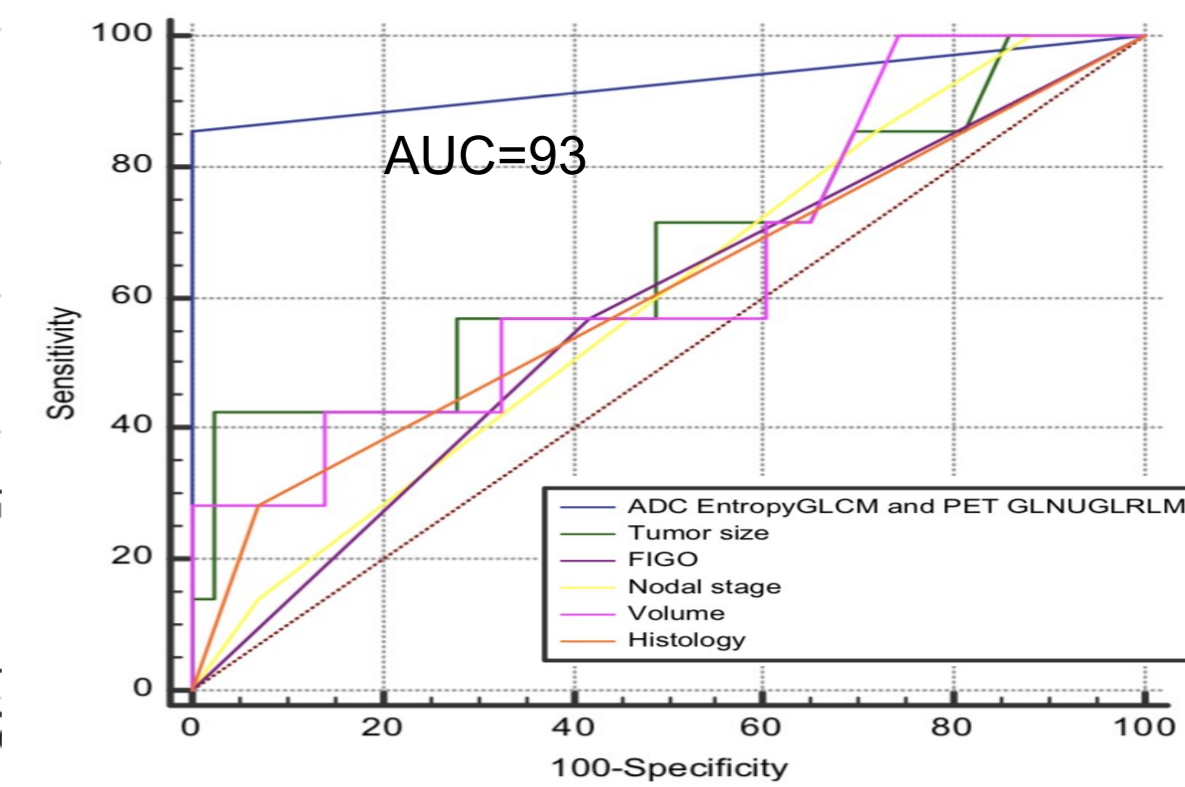
### Center 1 (validation)



### Center 2 (non-harmon)



### Center 2 (harmon)



## Inter-site and Intra-site model validation

Lucia, Eur J Nucl Med 2019, 2020