



# Physique et Imagerie Médicale

Paul Lecoq  
CERN, Genève

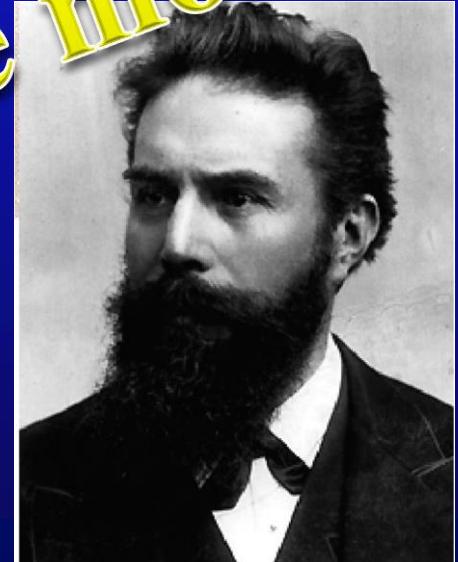
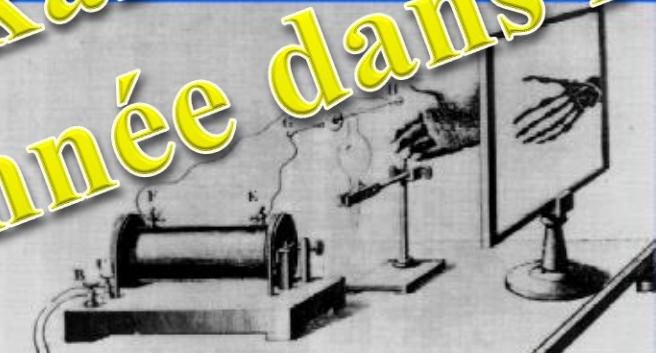
# La découverte des Rayons-X



• Le 8 Novembre 1895 Röntgen découvre les Rayons X

• Le 22 Novembre 1895 prend le premier cliché de la main de son épouse

500'000'000 d'examens RX chaque année dans le monde



Röntgen obtient le **1<sup>er</sup> prix Nobel de physique** en 1901

# Premières applications dans la thérapie du cancer

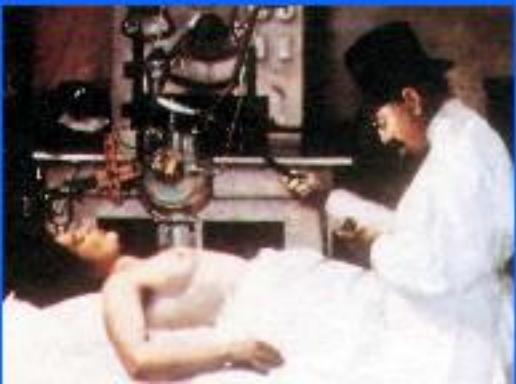
STOCKHOLM



1902

1912

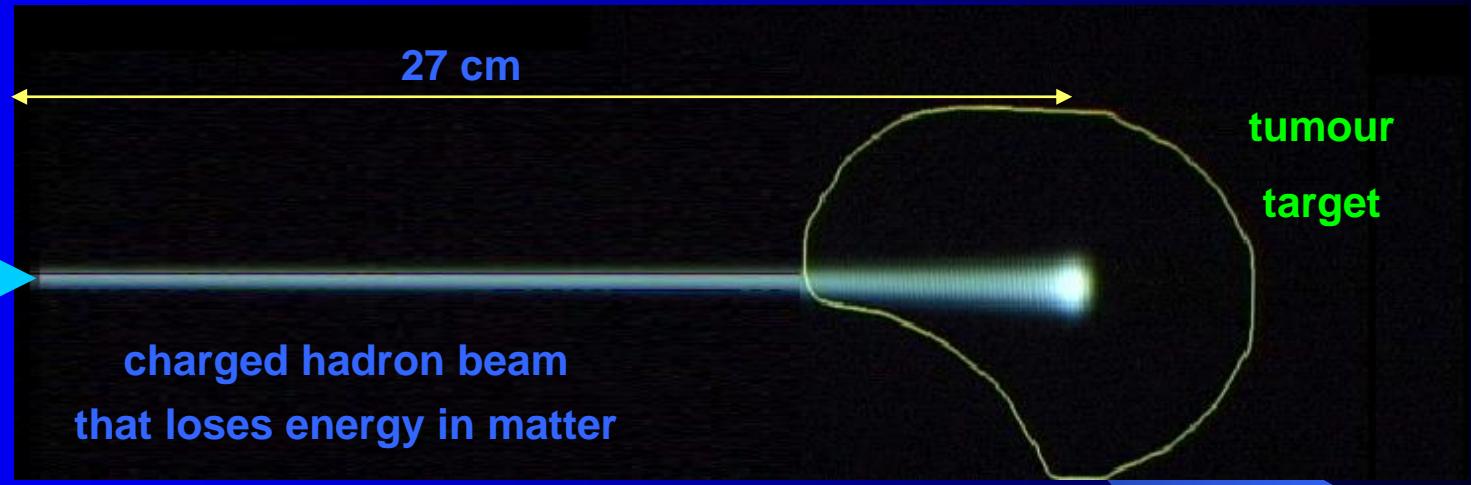
**Basic concept**  
**Local control  
of the tumour**



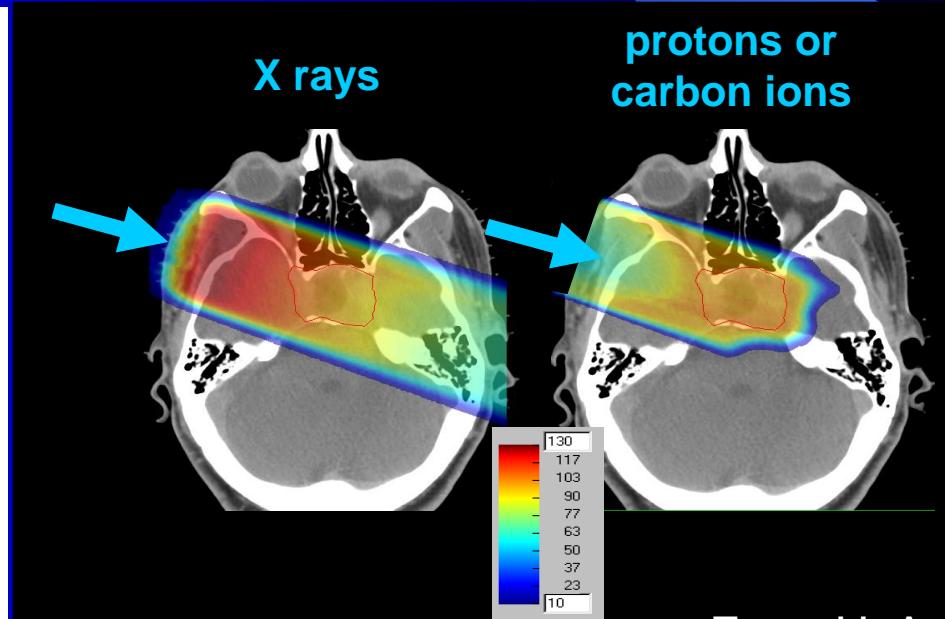
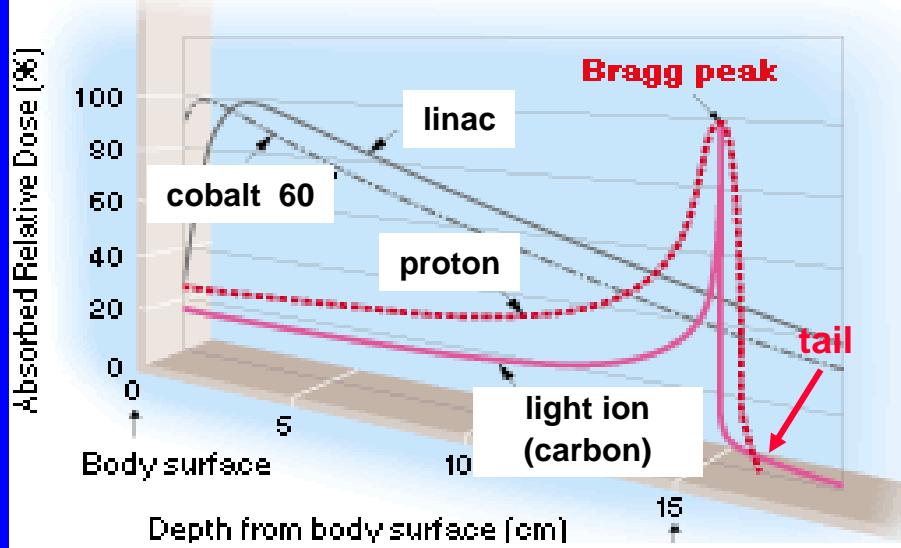
**1908 : first attempts of skin cancer radiation therapy in France ("Curitherapy")**

# Hadrontherapy accelerators the rationale

200 MeV - 1 nA  
 protons  
 4800 MeV – 0.1 nA  
 carbon ions  
which can control  
radioresistant  
tumours



[Dose Distribution Curve]





# Summary of accelerators running in the world



CATEGORY OF ACCELERATORS	NUMBER IN USE (*)
High Energy acc. ( $E > 1\text{GeV}$ )	~120
Synchrotron radiation sources	>100
<u>Medical radioisotope production</u>	<u>~200</u>
<u>Radiotherapy accelerators</u>	<u>&gt; 7500</u>
<u>Research acc. included biomedical research</u>	<u>~1000</u>
Acc. for industrial processing and research	~1500
Ion implanters, surface modification	>7000
<b>TOTAL</b>	<b><u>&gt; 17500</u></b>

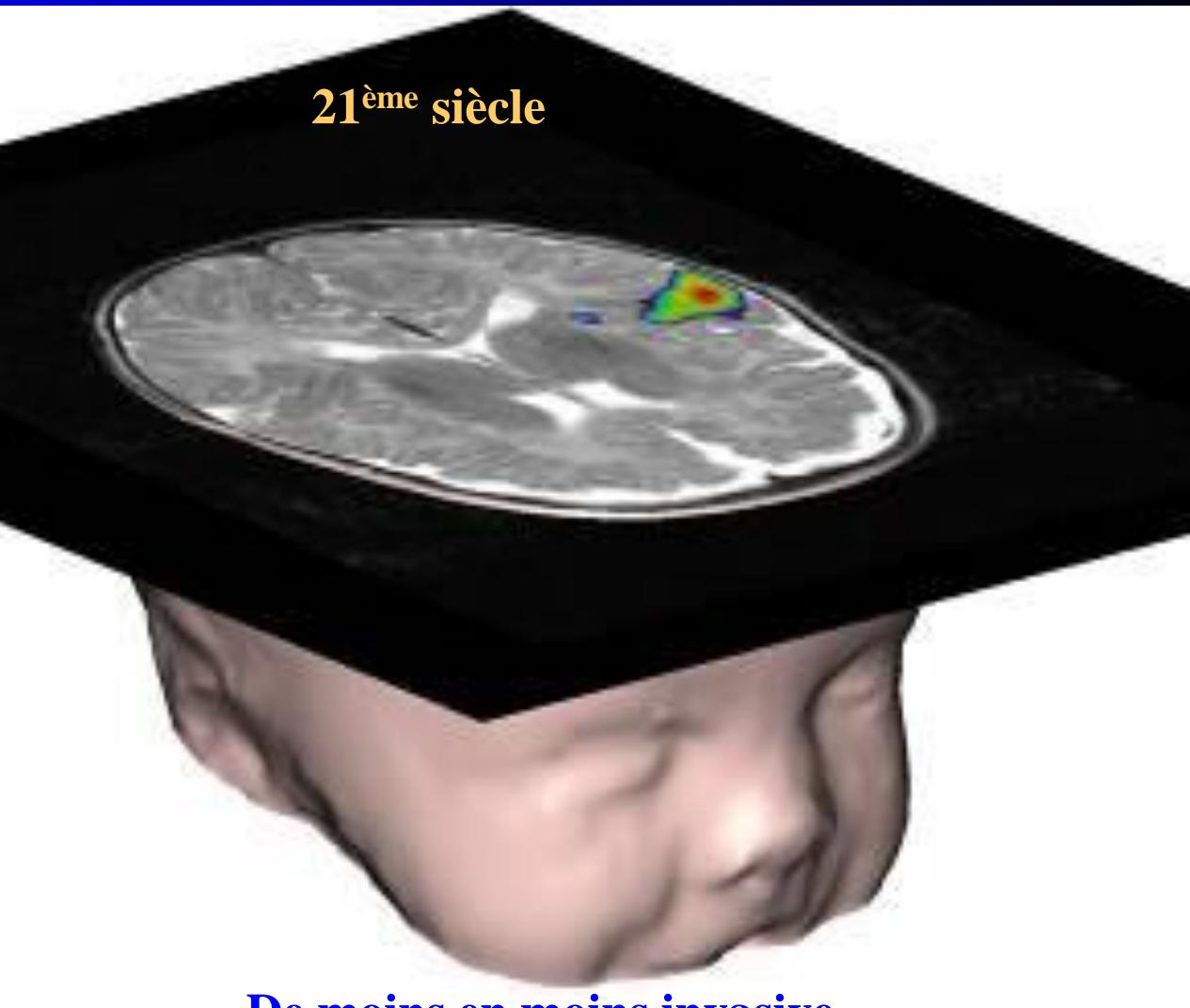
(\*) W. Maciszewski and W. Scharf: Int. J. of Radiation Oncology, 2004

# Petite histoire résumée de l'imagerie in-vivo

20<sup>ème</sup> siècle

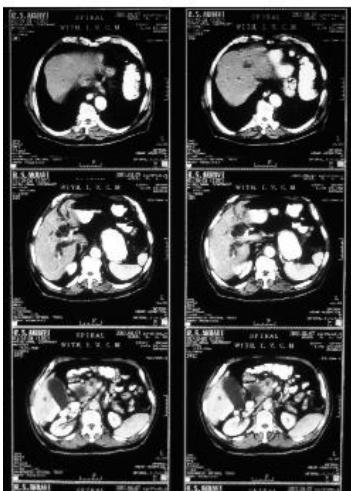


21<sup>ème</sup> siècle



**De moins en moins invasive**

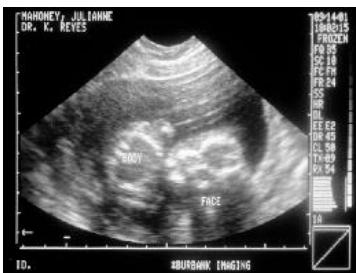
# Imaging Modalities



**A** Tissue Density,  
20-50  $\mu\text{m}$

**CT**

## Ultrasound



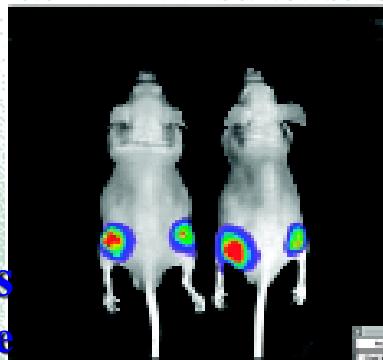
**A** **F**

Structure  
0.1 mm  
Doppler

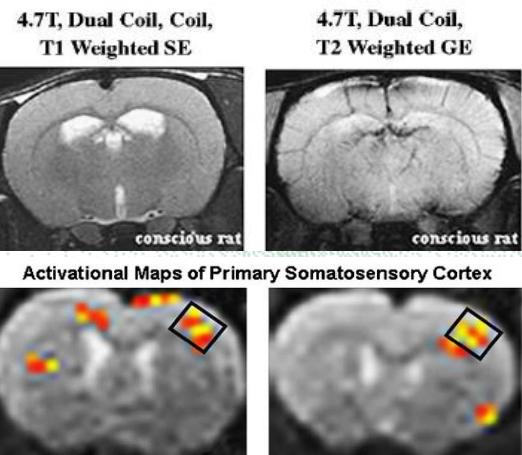
## Optical (Bioluminescence, fluorescence)

**A** **M**

Topography  
 $\mu\text{m}$  to mm  
 $\sim 10^3$  cells  
 $\neq$  quantitative



Photons involved



**MRI**

**A** **F** **M**

H Concentration  
0.1 mm

**BOLD, DCE**

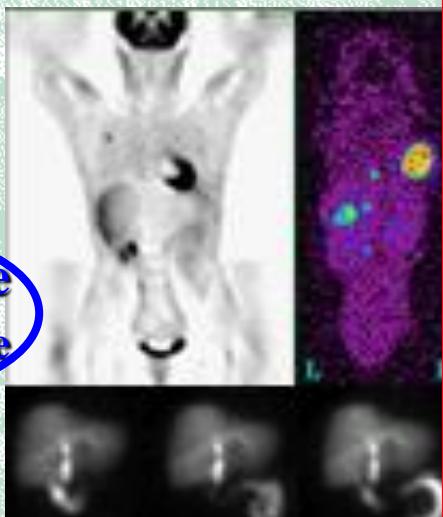
$\beta$ -galactocidase

0.1 umole H / umole  $^{31}\text{P}$

## PET/SPECT

**F** **M**

Radiotracer  
 $\sim 1-2$  mm  
 $< 10^{-12}$  mole  
 $=$  quantitative



# L'imagerie pour une meilleure prise en charge du patient

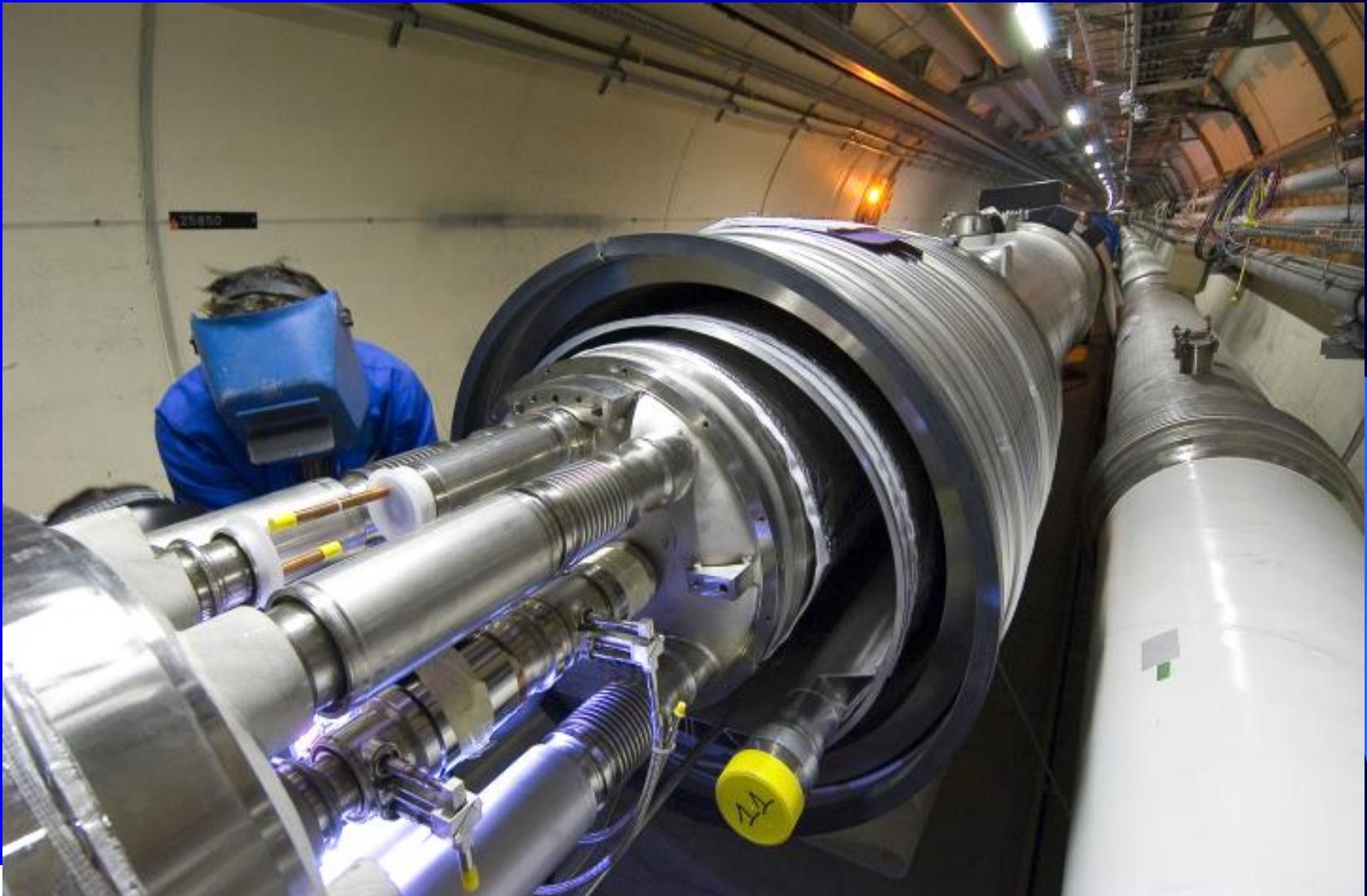
Recueillir une information détaillée de chaque individu pour:



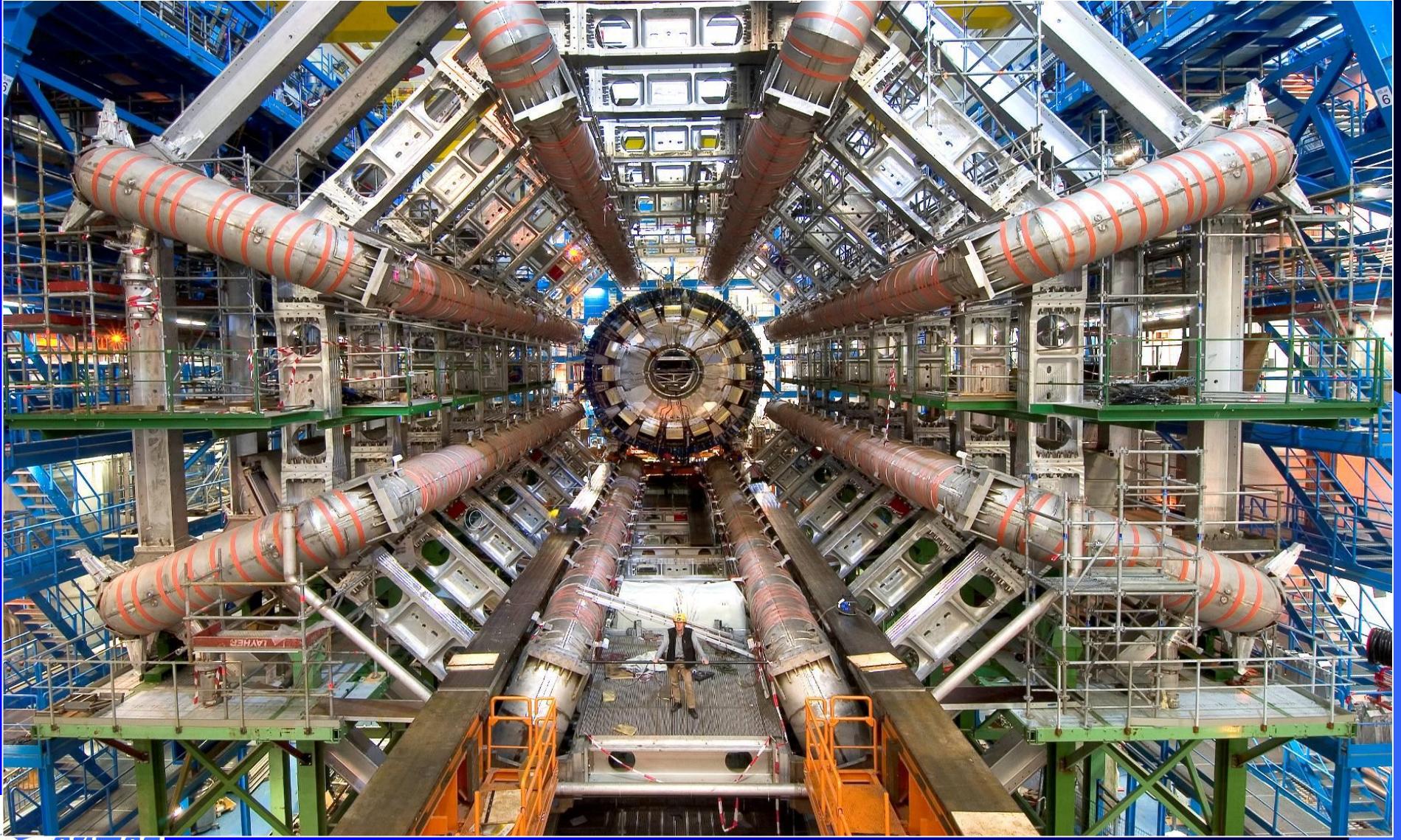
- Diagnostiquer la maladie à un stade précoce
- Déterminer les paramètres de la maladie, comme son agressivité, son potentiel métastasique
- Optimiser l'action thérapeutique en fonction du génotype du patient
- Evaluer instantanément l'efficacité du traitement

*Implique une nouvelle génération  
de systèmes d'imagerie*

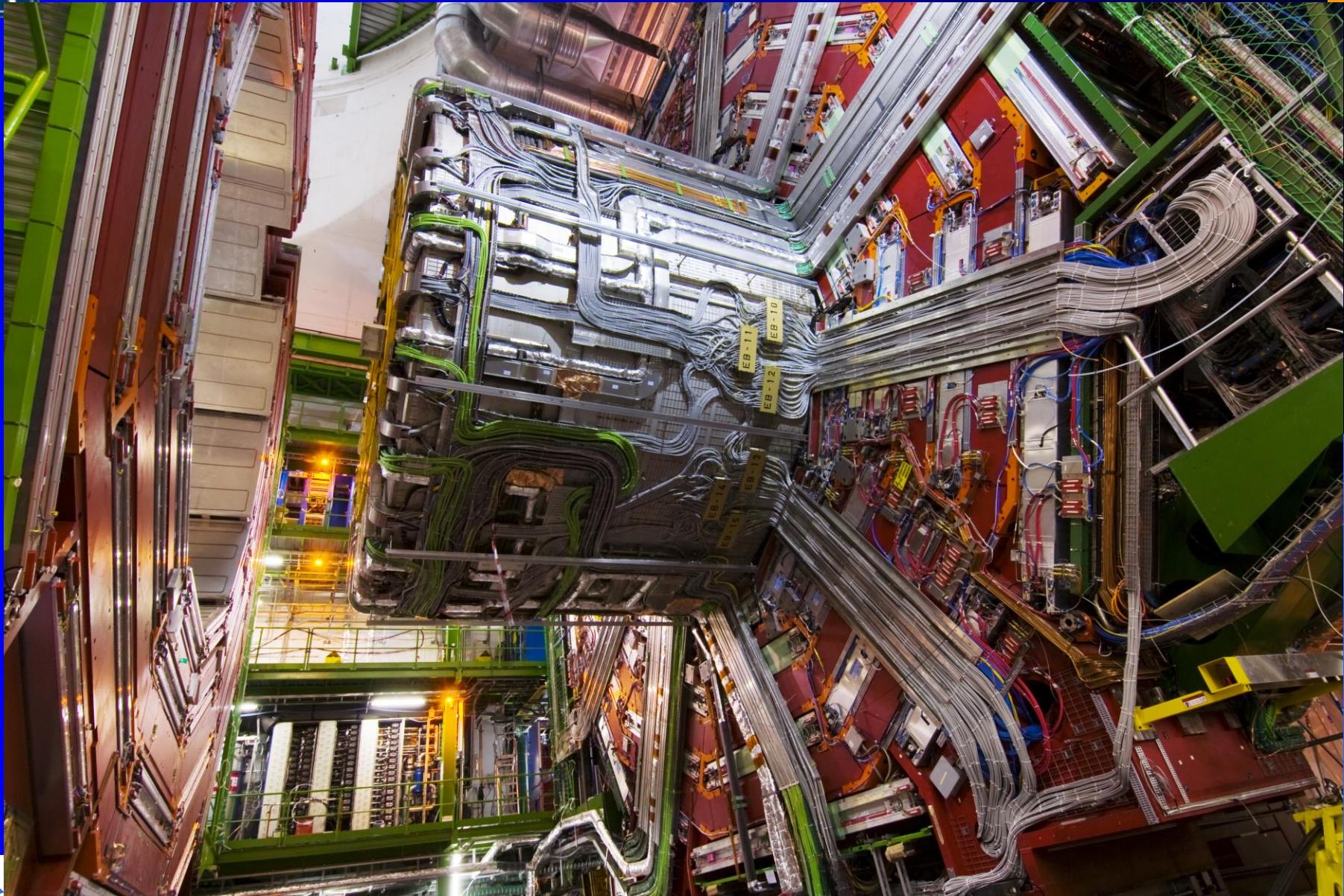
# LHC - Installation des aimants supraconducteurs (27km)



# L'aimant toroïdal d'Atlas



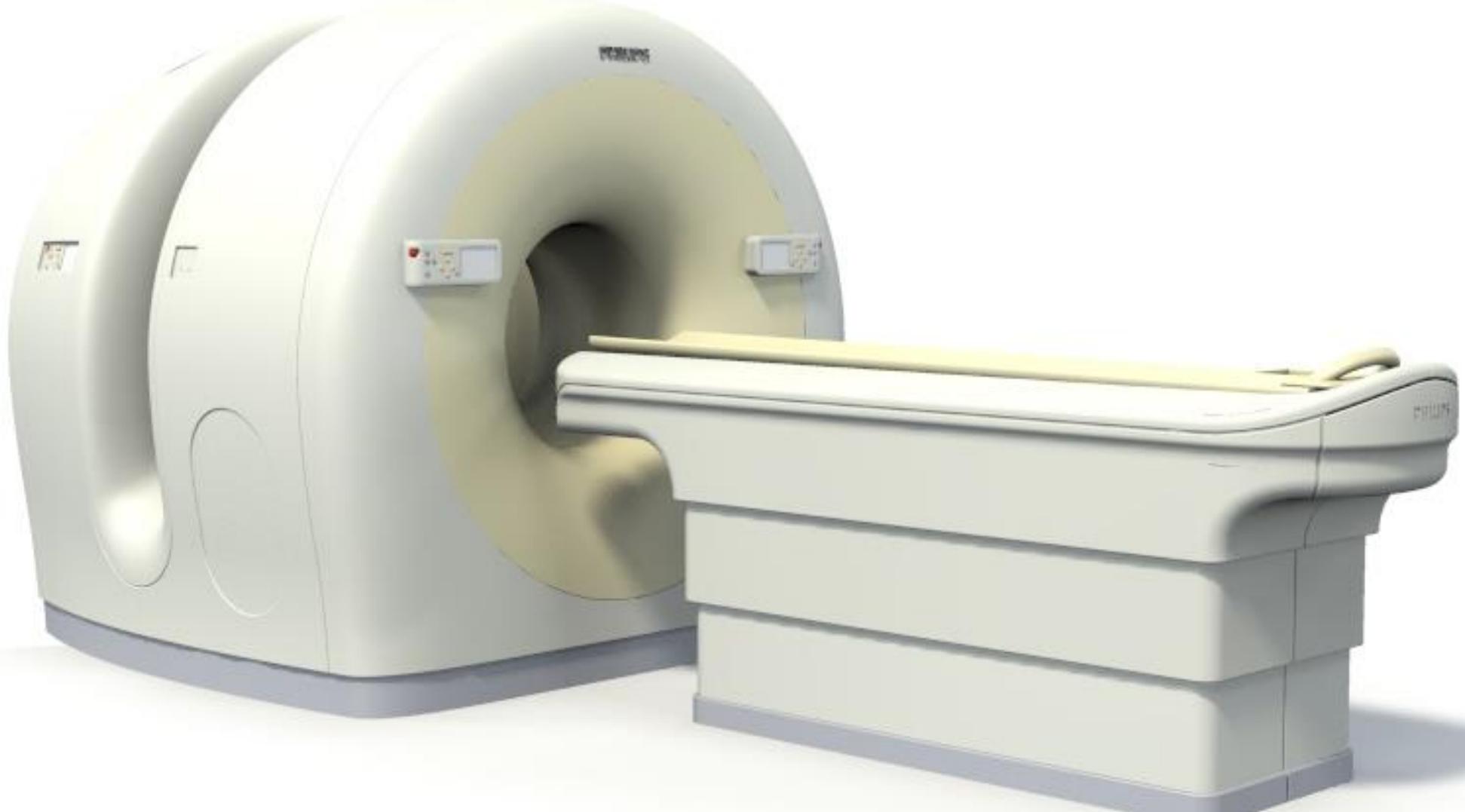
# Montage de l'expérience CMS



# Simulation de la désintégration d'un boson de Higgs dans CMS



# Scanner TEP/CT



# Imagerie anatomo-fonctionnelle non invasive



Pati<sup>e</sup>nte trait<sup>ée</sup>  
pour un cancer  
du colon  
r<sup>é</sup>v<sup>él</sup>ant <sup>à</sup>  
l'examen un  
cancer du sein  
additionnel

# L'imagerie médicale: une approche pluridisciplinaire

Physique



Mathématiques

$$\int (x + \cos x + \tan x) dx = 0$$
$$\sin^2 \alpha = \frac{1 - \cos^2 \alpha}{2}$$

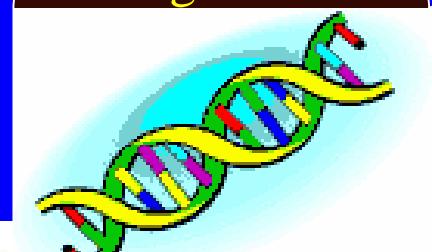
Médecine



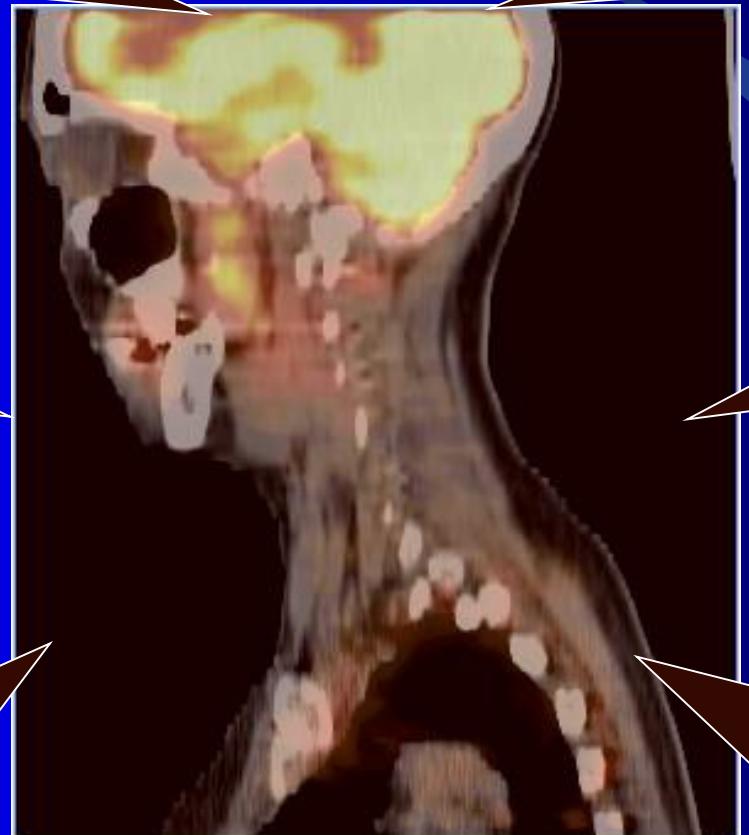
Chimie



Biologie



Informatique



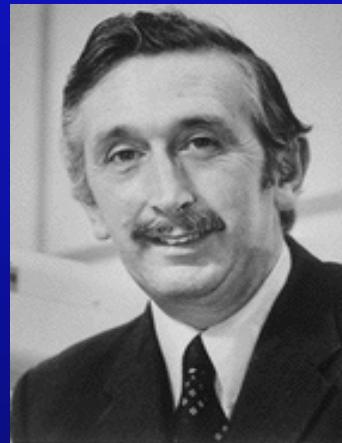
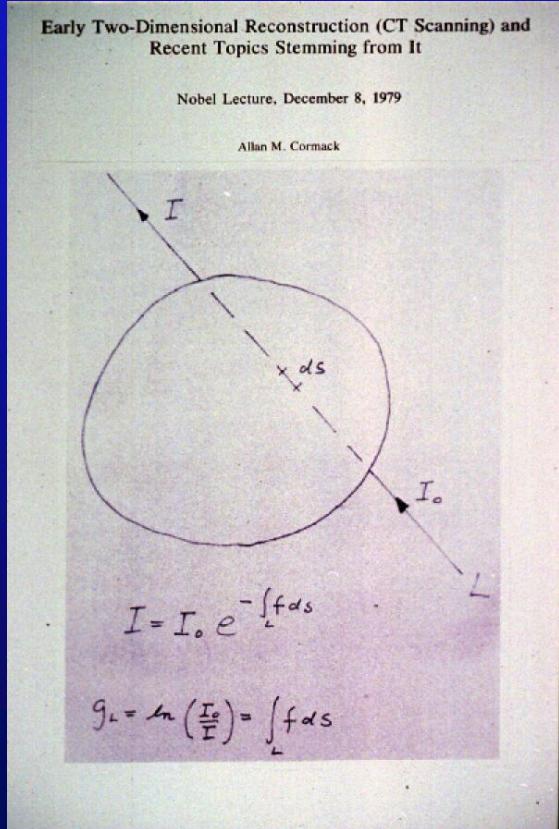
# CAT Scanner

## Le principe de la tomographie

### Prix Nobel de Physiologie et Médecine 1979

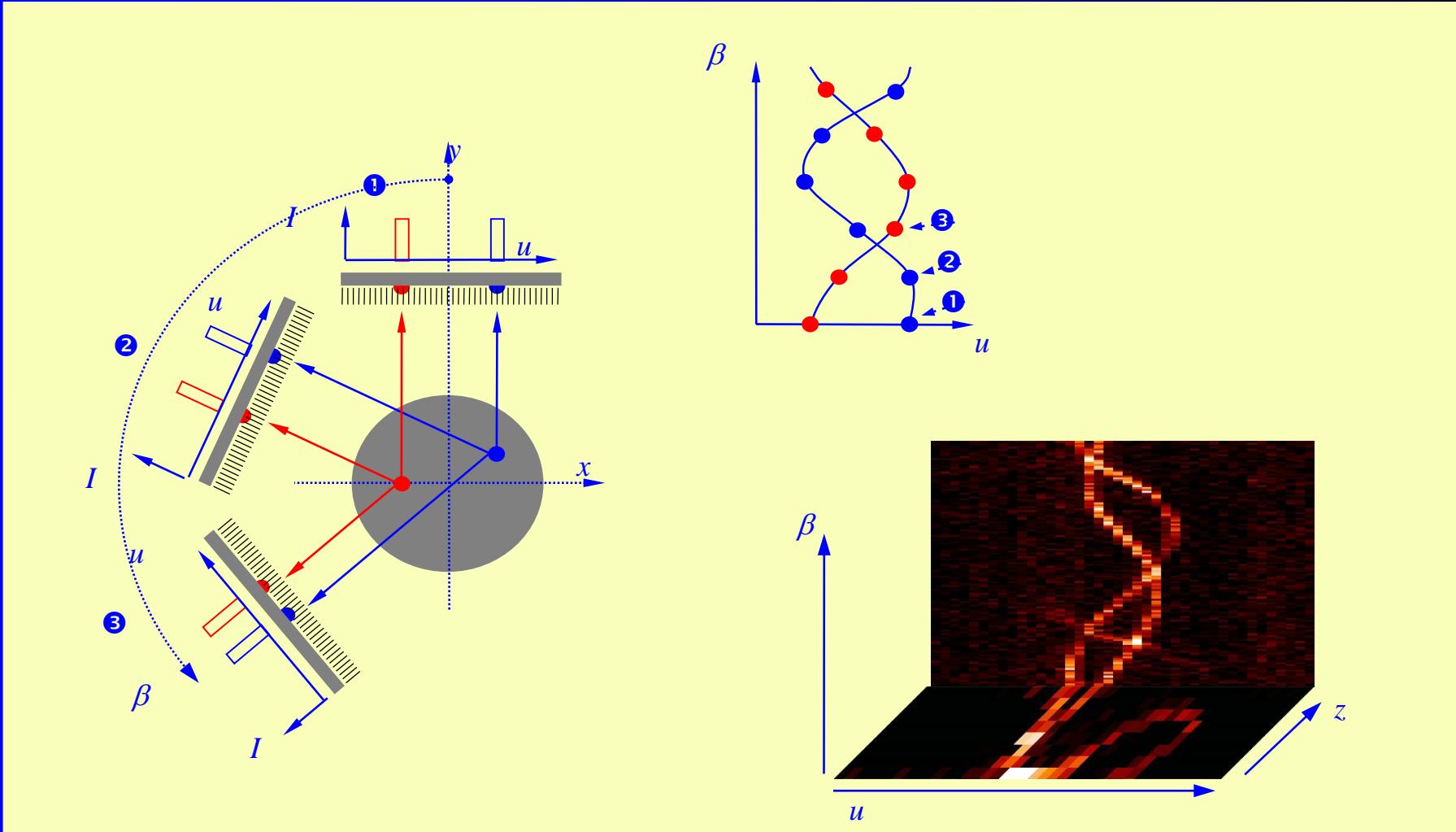


Allan MacLeod **Cormack**  
Physicien Nucléaire  
Cape Town  
Harvard University  
Tufts University



Sir Godfrey N. **Hounsfield**  
Ingénieur électrique anglais  
EMI Research

# Principle of CT

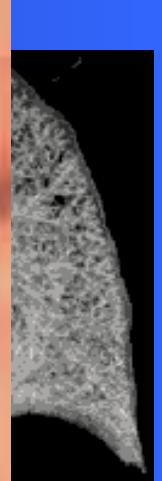




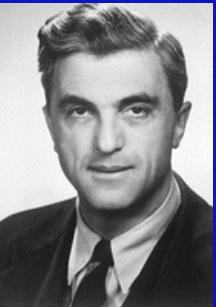
# Volumetric CT



/sec)

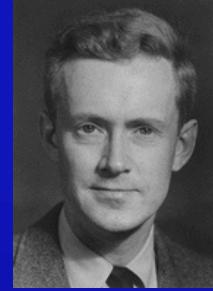
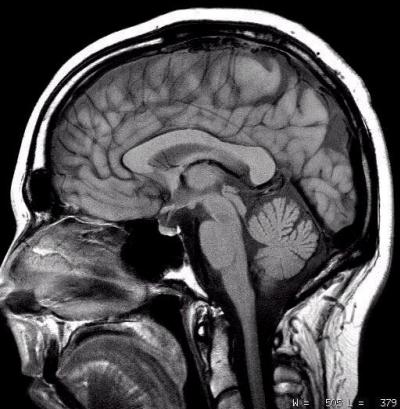


# IRM, imagerie par résonance magnétique



Felix Bloch  
Physicien Stanford

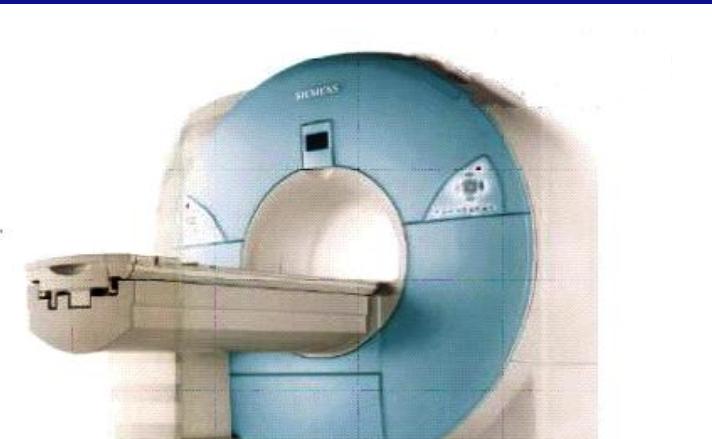
## Prix Nobel de Physique 1952



Edward M. Purcell  
Physicien Harvard



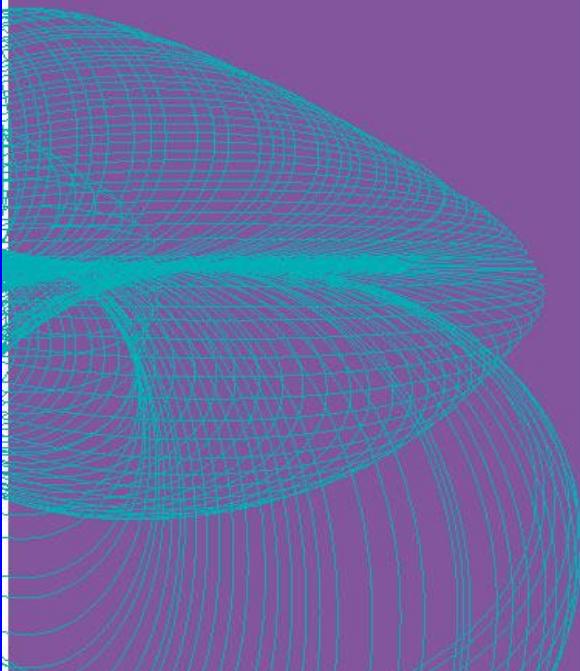
Sir Peter Mansfield  
Physicien Nottingham



Paul C. Lauterbur  
Chimiste Uni. Illinois

# Un peu d'histoire

# 1977

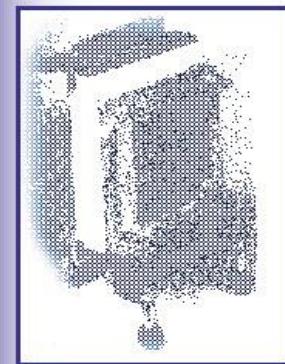


CERN Technology Transfer

<http://cern.ch/TTdb>

## *when PET started at CERN*

SCAN OF MOUSE SKELETON :  $5.7 \mu\text{Ci}$ ,  $\text{F}^{18}$  (position emission)  
1 bin = 1 mm x 1 mm. Plane spacing = 4 mm.

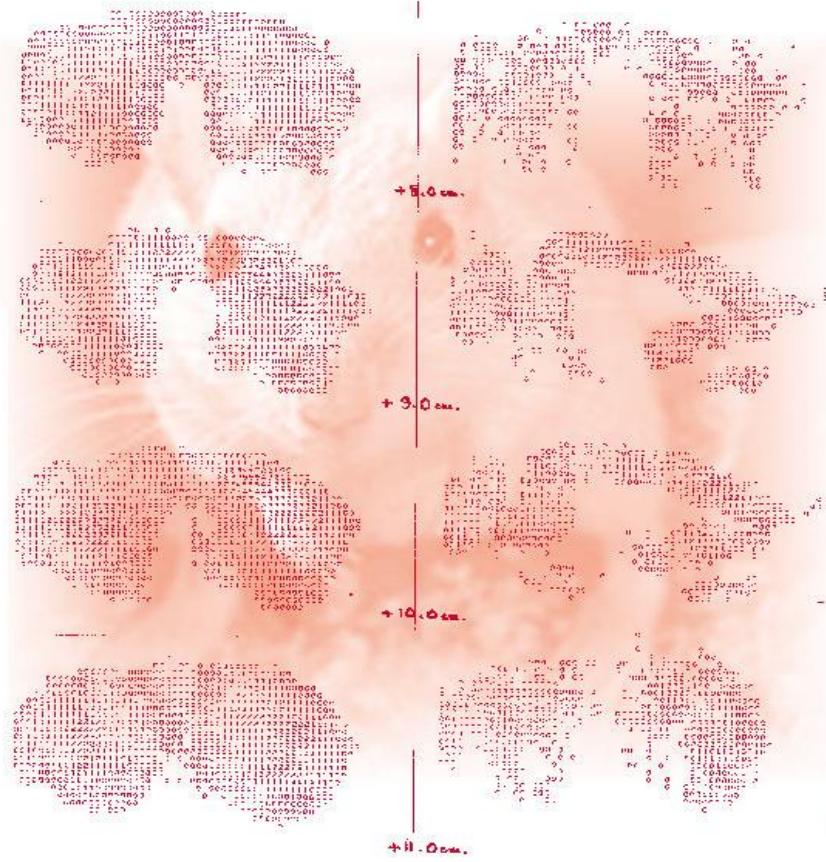


(Jenane, Townsend et al.)  
Spatial resolution 2.4 mm FWHM  
Maximum data rate: 3000 c.p.s.  
Sensitivity: 25 c.p.s./ $\mu\text{Ci}$   
 $1 \mu\text{Ci}=3.7 \times 10^4 \text{Bq}$

TOMOGRAM

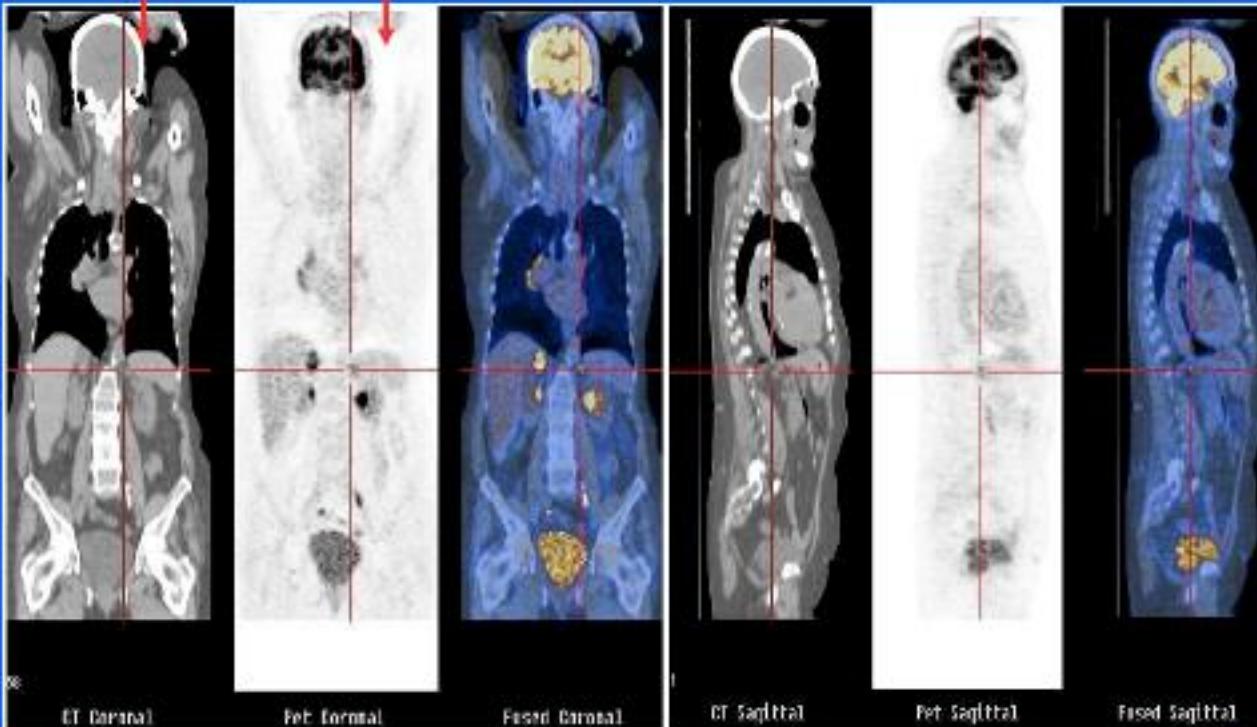


RECONSTRUCTION



# Combiner les informations anatomique et fonctionnelle

**morphology      metabolism**



**David Townsend**

**CERN: 1970-78**

**Université de Genève**

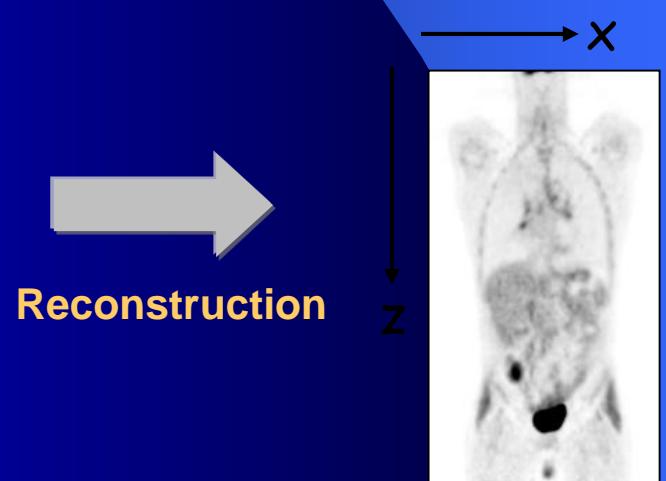
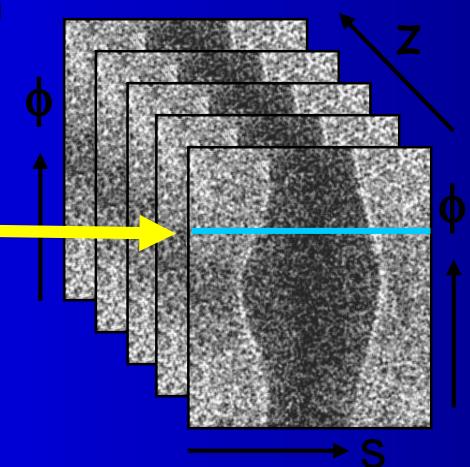
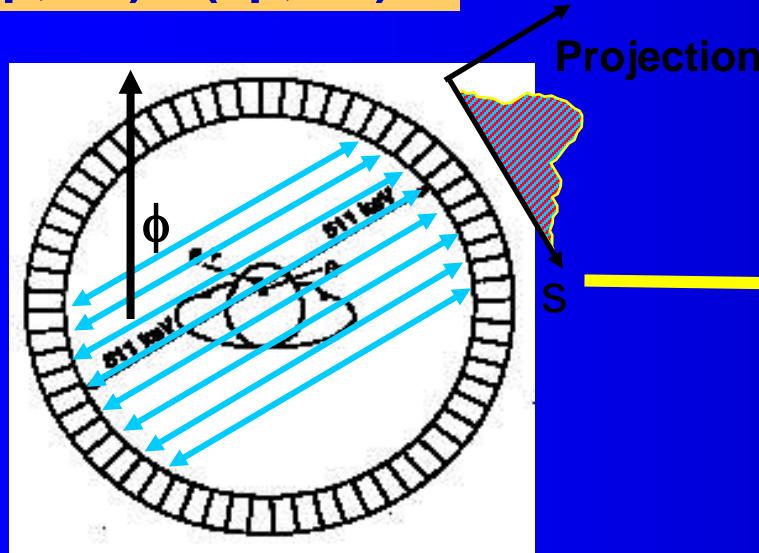
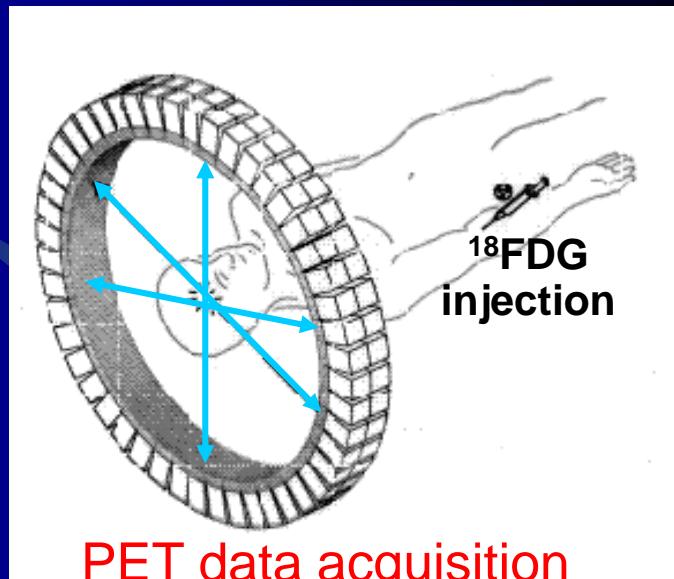
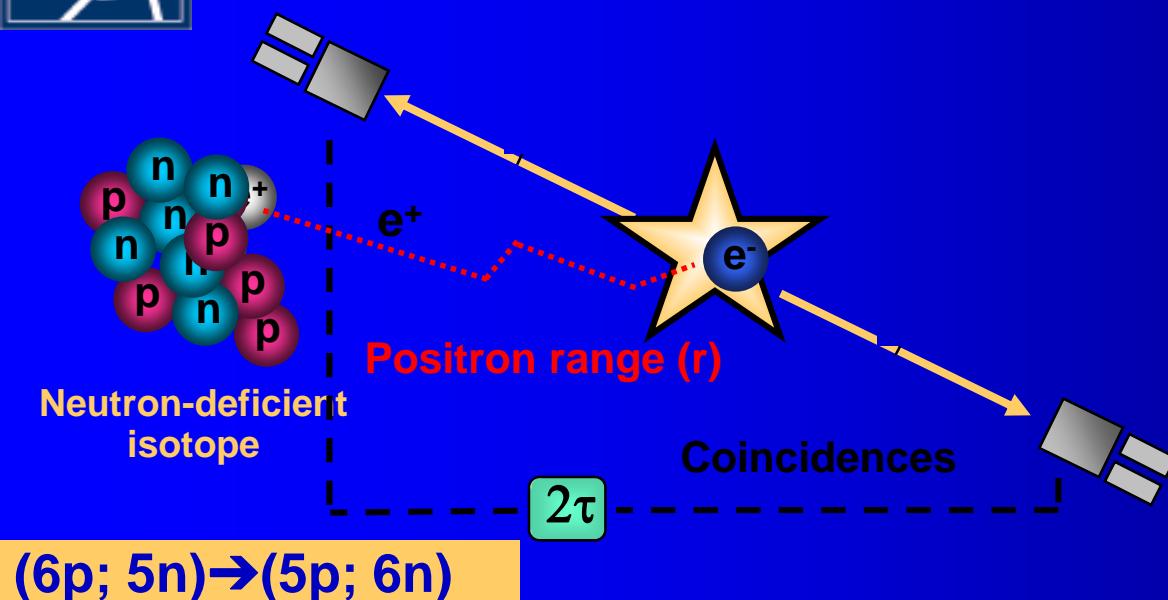
**UPSM Pittsburgh**

**and**

**Ronald Nutt**

**(CTS – CTI)**

# PET Principle



# Des défis similaires pour l'imagerie TEP et les détecteurs de physique

## Cahier des charges pour la physique

### 1. Cristaux

- Densité élevée ( $> 6 \text{ g/cm}^3$ )
- Emission rapide ( $< 100 \text{ ns}$ ), spectre visible
- Emission lumineuse modérée à élevée
- Excellente résistance aux radiations

Transfert technologique

### 2. Photodetecteurs

- Compact
- Grande efficacité quantique et gain élevé
- Grande stabilité

Transfert technologique

### 3. Electronique de lecture

- Mise en forme rapide du signal, faible bruit
- Fortement intégrée

Transfert technologique

### 4. Architecture d'acquisition DAQ

- Intégrée et parallèle, temps mort réduit

### 5. Logiciels

- Simulation précise par Monte Carlo

Transfert technologique

### 6. Integration

- Systèmes compacts avec un très grand nombre de canaux ( $> 10'000$ )

Transfert technologique

Transfert technologique

## Cahier des charges pour l'imagerie médicale

### 1. Cristaux

- Densité élevée ( $> 7 \text{ g/cm}^3$ )
- Emission rapide ( $< 100 \text{ ns}$ ), spectre visible
- Emission lumineuse élevée
- Résistance modérée aux radiations

### 2. Photodetecteurs

- Compact
- Grande efficacité quantique et gain élevé
- Grande stabilité

### 3. Electronique de lecture

- Mise en forme rapide du signal, faible bruit
- Fortement intégrée

### 4. Architecture d'acquisition DAQ

- Intégrée et parallèle, temps mort réduit

### 5. Logiciels

- Simulation précise par Monte Carlo

### 6. Integration

- Systèmes compacts avec un très grand nombre de canaux ( $> 10'000$ )



# The PET World Picture

Need to Image  
**0.000000511 TeV\***  
Photons

\*511 keV

**Signal Levels Are Very Low**



# L'imagerie: quelle qualité pour voir quoi?





# Limite liée à la résolution de l'instrument





# Limite liée au bruit de fond



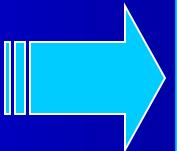


# Cas réel: combinaison des 2 effets



# L'imagerie médicale du futur

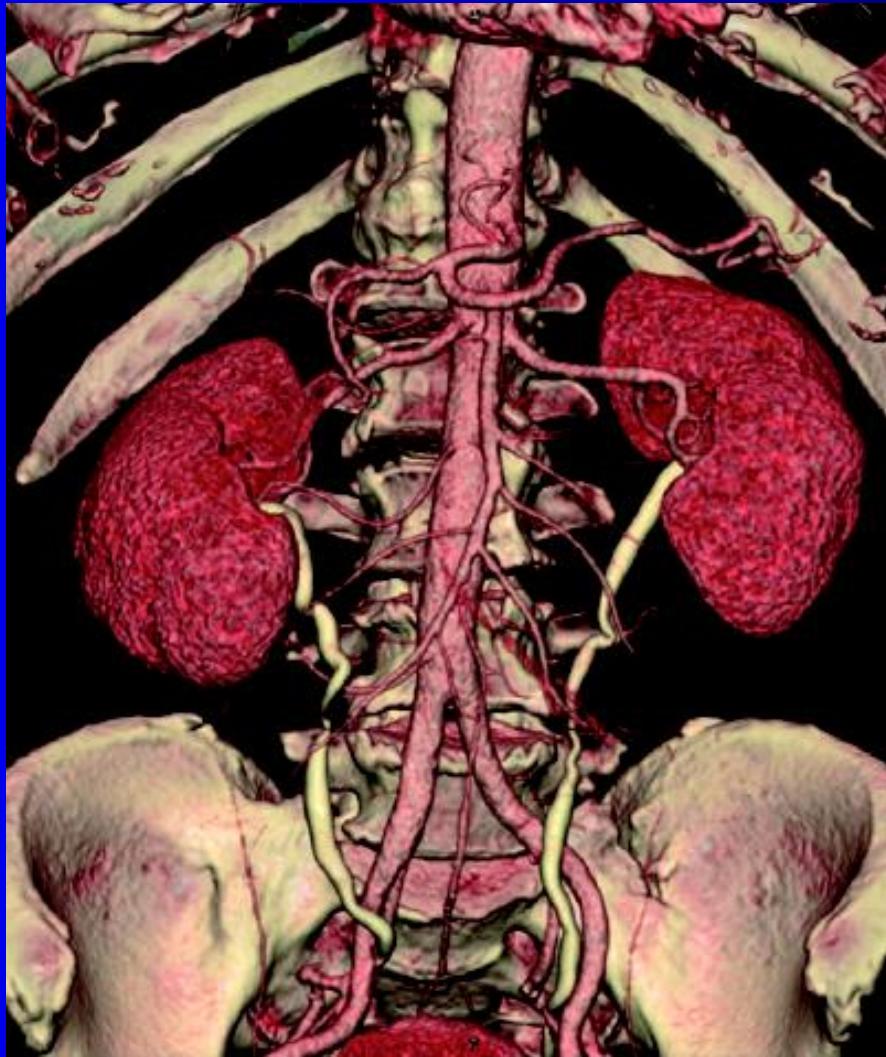
- Examens plus rapides
- Correction de mouvements
  - Respiration
  - Battements cardiaques
  - Bolus digestif
- Etudes dynamiques
- Quantification
- Multimodalité
- Réduire la dose aux patients



## AMELIORER

- Résolution spatiale
- Résolution temporelle
- Sensibilité
- Rapport Signal/Bruit

# La quête pour une meilleure résolution spatiale



Siemens Somatom CT 64 slices

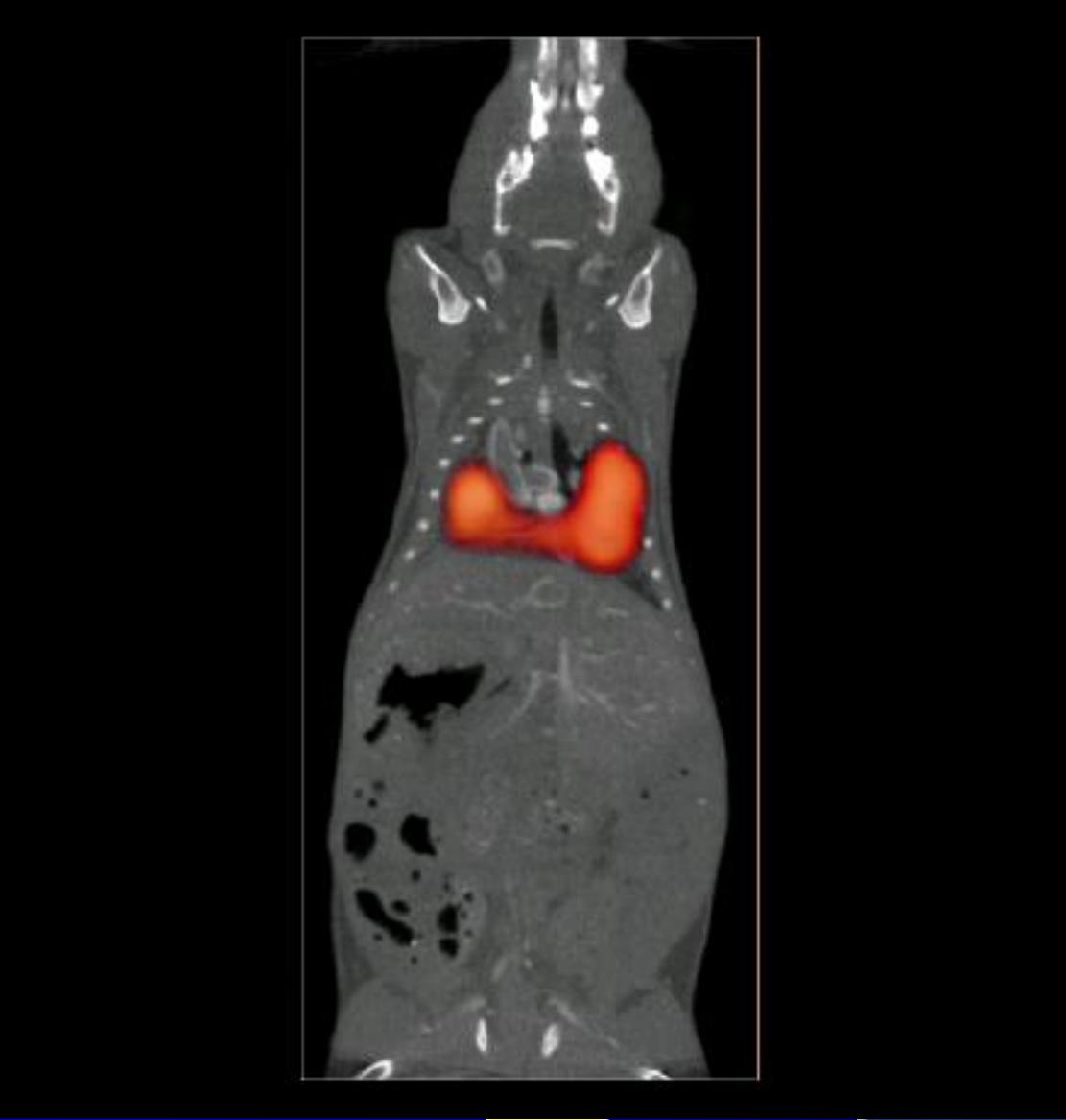
CERN – French Physics Teachers – 20 Octobre 2015

P. Lecoq CERN

# Trends in medical imaging

- Small animal imaging
  - Large variety of transgenic animals (mainly rodents) to model different disease
  - Repetitive observations of biological processes on the same animal
  - Assess effectiveness of new diagnostics, prevention and therapeutic strategies
  - Develop new drugs

# La quête pour une meilleure compréhension de la matière



(x 300)  
0)

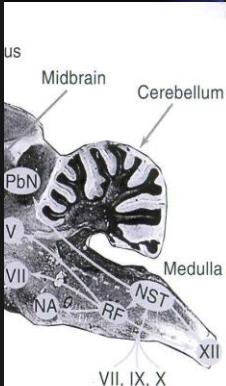
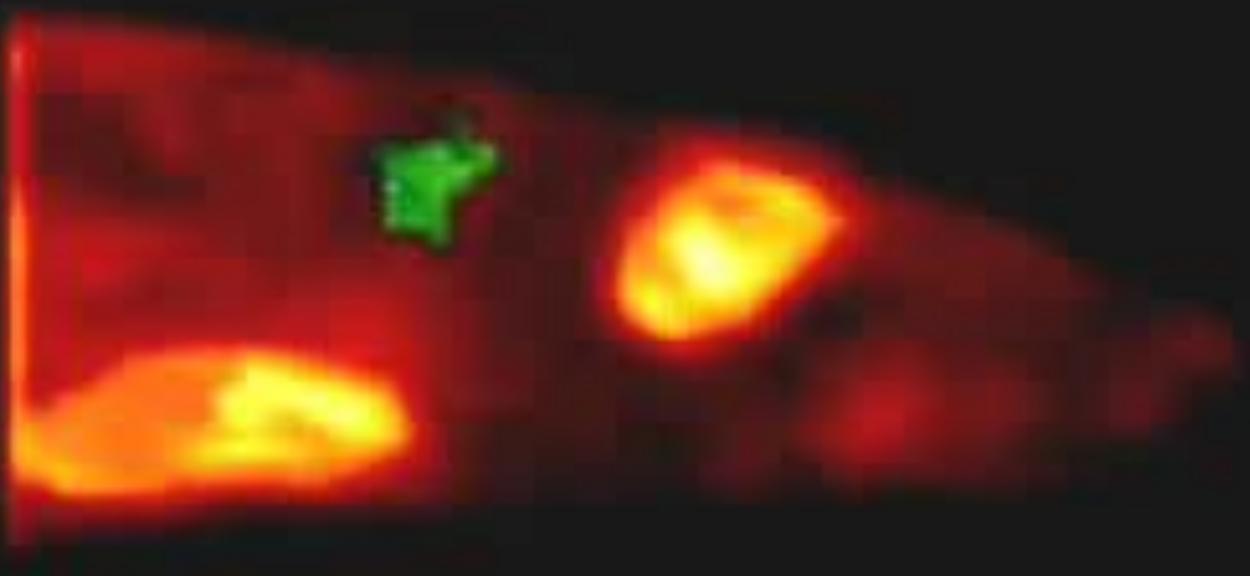
x réclame des  
gration et à



# ClearPET®, TEP petit animal



ebellum



# Etudes de plus en plus spécifiques sur modèles animaux

- L'imagerie petit animal se fait généralement sous anesthésie
- L'anesthésie modifie les fonctions cervicales et biaise les études neurophysiologiques
- RATCAP, développé à BNL est un TEP miniaturisé et portable pour animal éveillé
- 12 blocs de 4x8 cristaux de LSO  $2 \times 2 \times 5 \text{ mm}^3$  lus par des matrices de 4x8 APD et  $0.18 \mu\text{m}$  CMOS ASIC
- C. Woody et al. Several papers in conference records of NSS/MIC2004, Rome

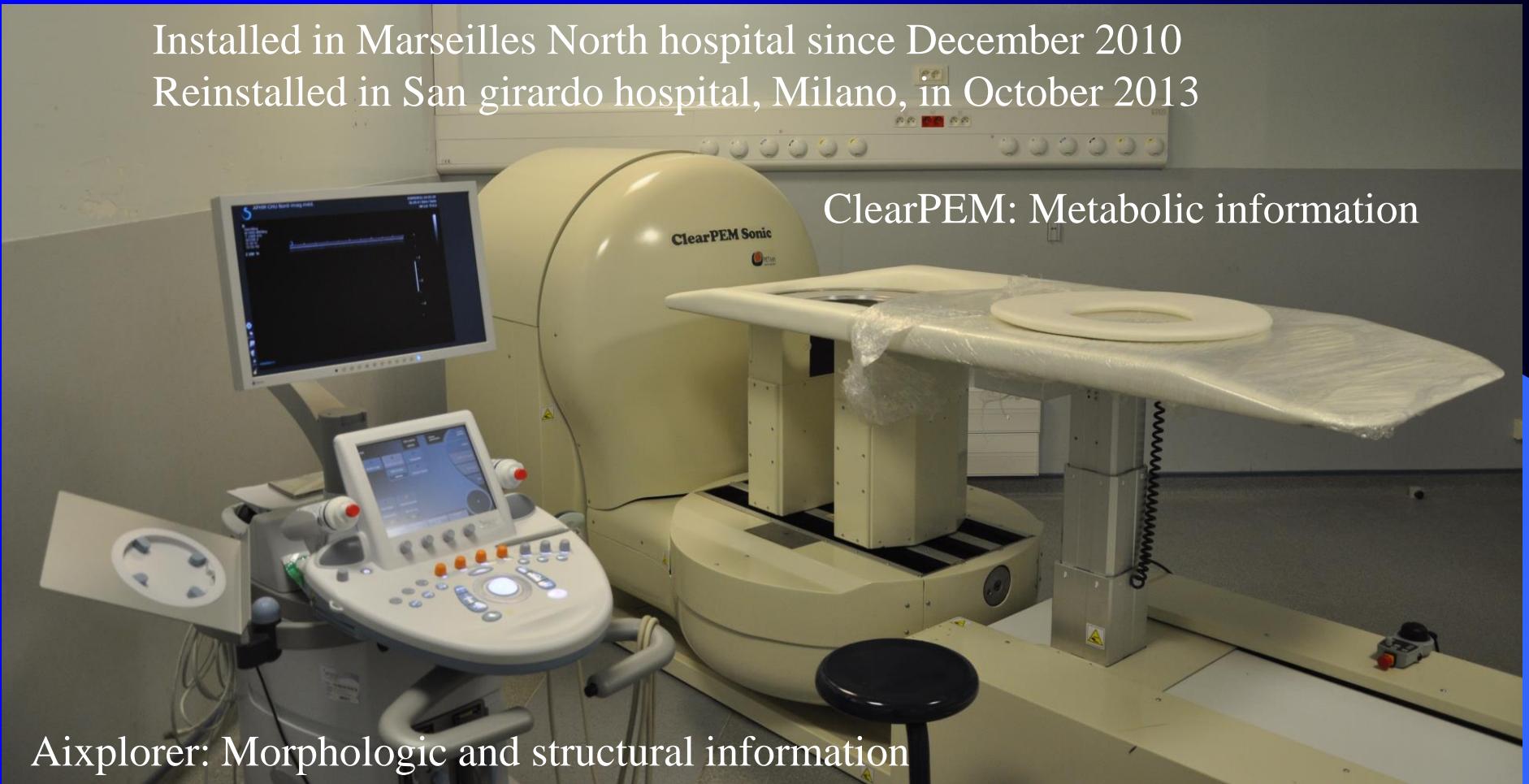


*Courtesy of C. Woody, BNL*

# ClearPEM-Sonic a collaborative project between physicians and physicists

Installed in Marseilles North hospital since December 2010  
Reinstalled in San girardo hospital, Milano, in October 2013

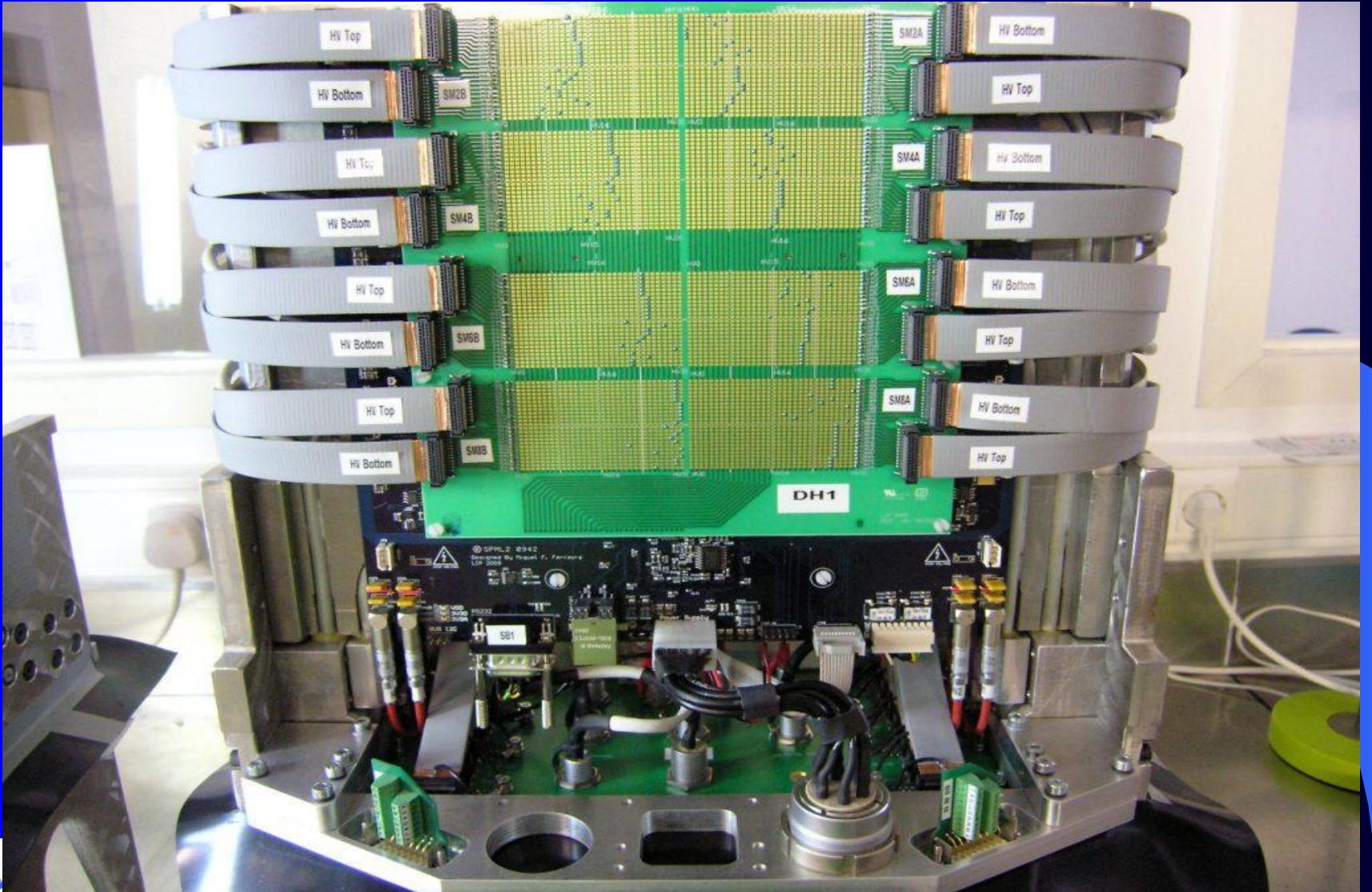
ClearPEM: Metabolic information



Aixplorer: Morphologic and structural information

*Objective: Detect 3mm tumors and define their cancerous status*

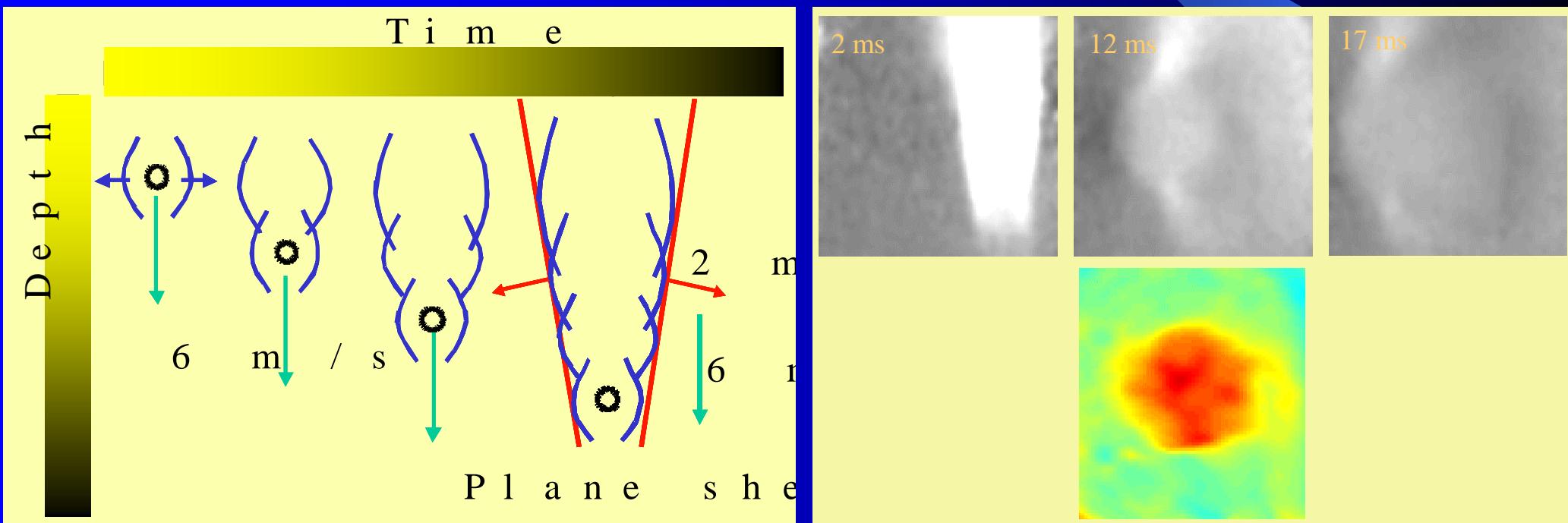
# Des technologies d'avant-garde ClearPEM



# New technologies

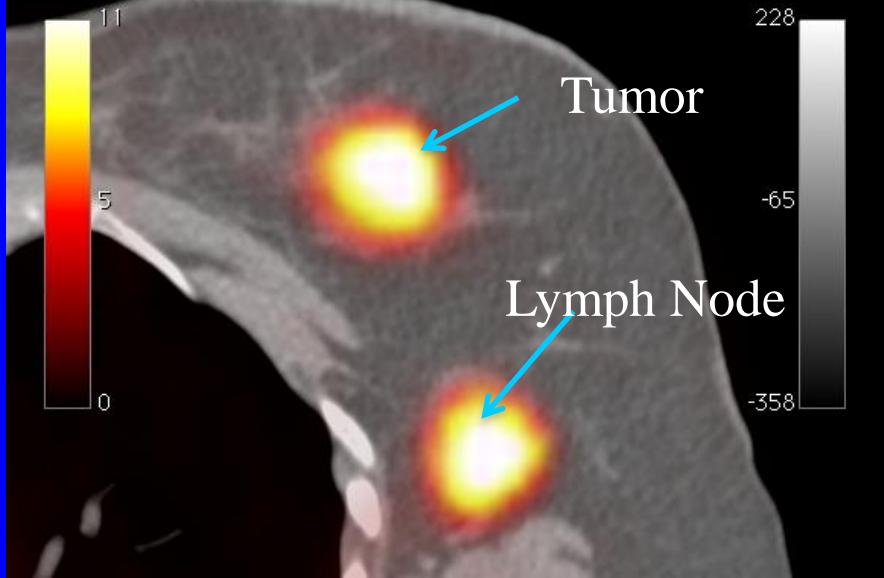
## Ultrasound

- Focus ultrasound beam in tissue
- Propagate focal point at supersonic speed in breast
- Measure the deformation of the shock wave by a tumor

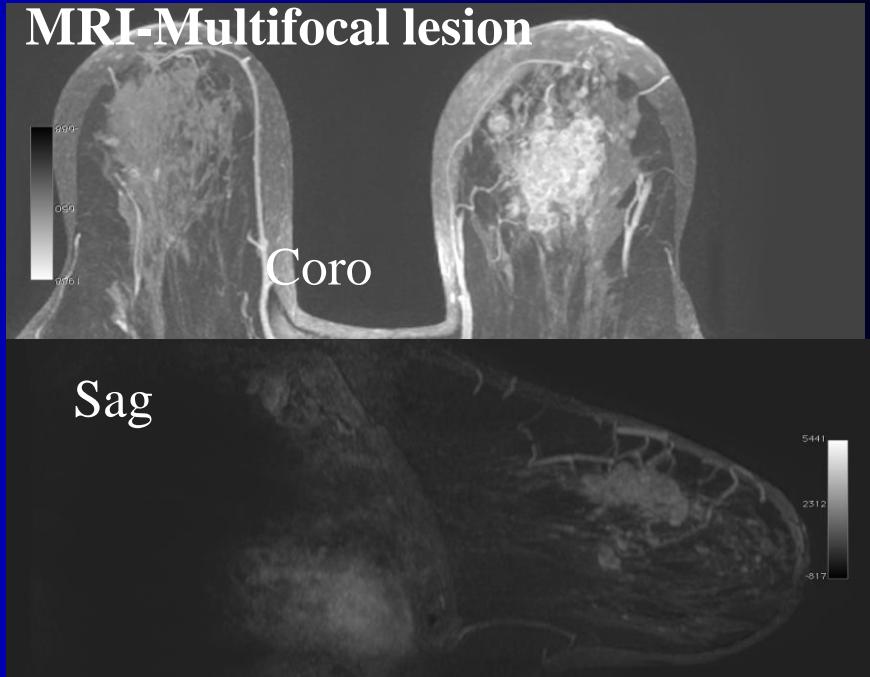


# Benefit of dedicated breast PET imaging

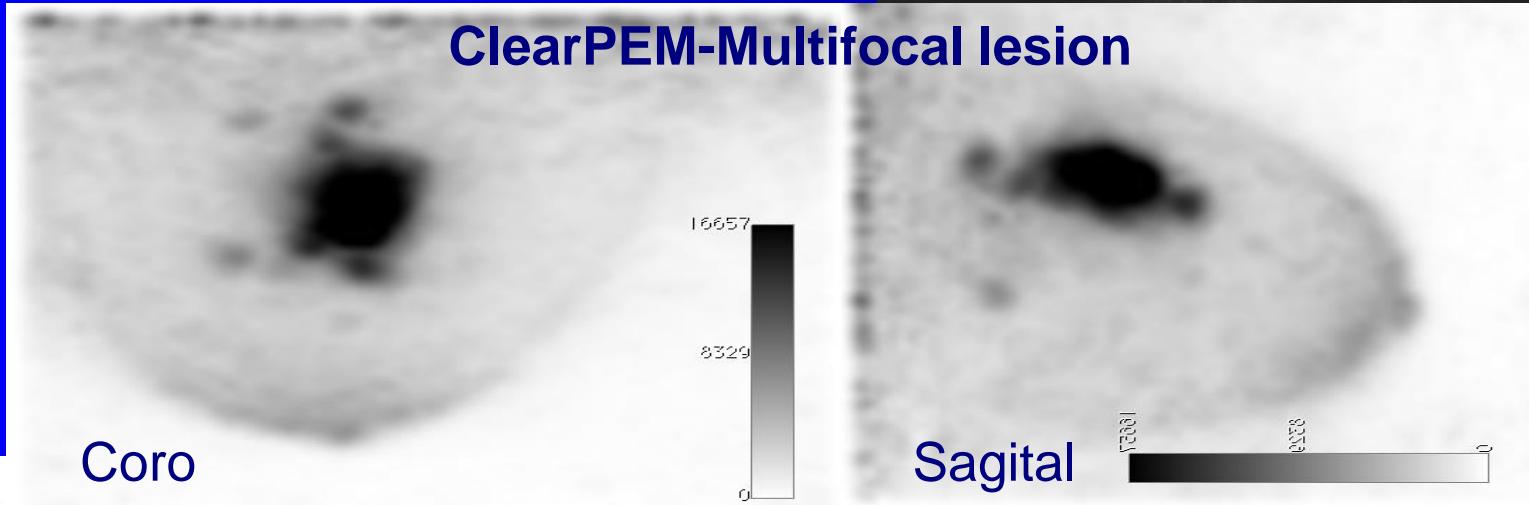
PET Whole Body (AC and Fused)



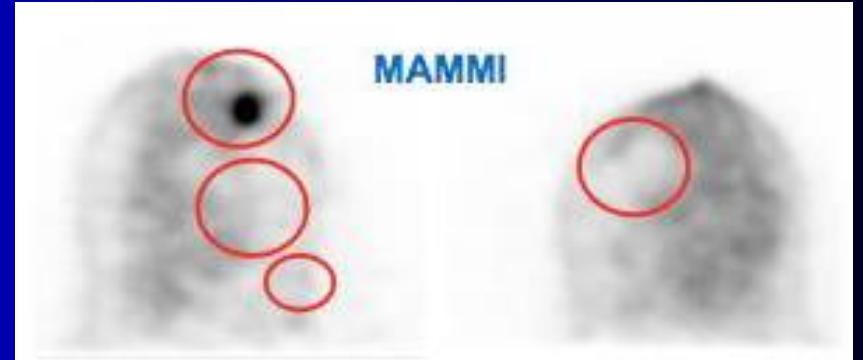
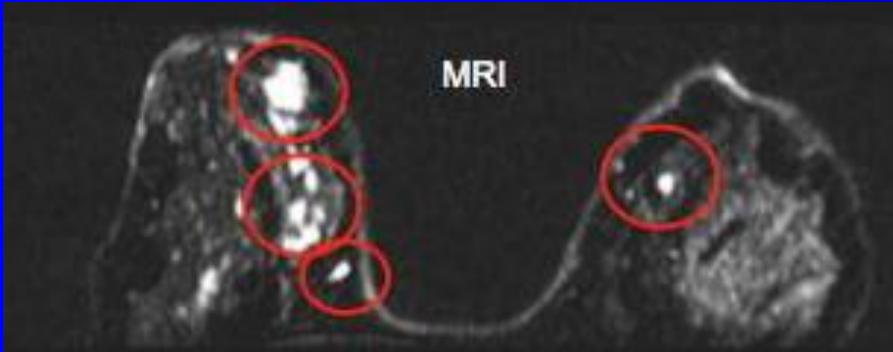
MRI-Multifocal lesion



ClearPEM-Multifocal lesion



# PET/MRI complementarity

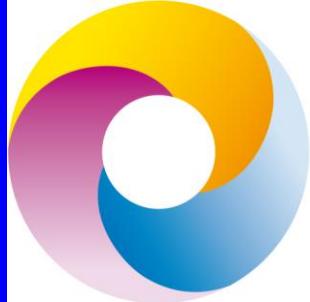


4 lesions identified on MR image

Only one suspicious lesion identified on PET image

Subsequent biopsy and histology of all four lesions confirmed that only the lesion seen on PET image was cancerous

*Courtesy: Dr. José Ferrer, ERESA, Hospital General Universitario de Valencia, Spain*



# ENDO TOFPET US

Endoscopic TOFPET & Ultrasound

*Novel multimodal endoscopic probes for simultaneous PET/ultrasound imaging for image-guided interventions*

FP7 project, call Health 2010

P. Lecoq  
CERN, Geneva, Switzerland

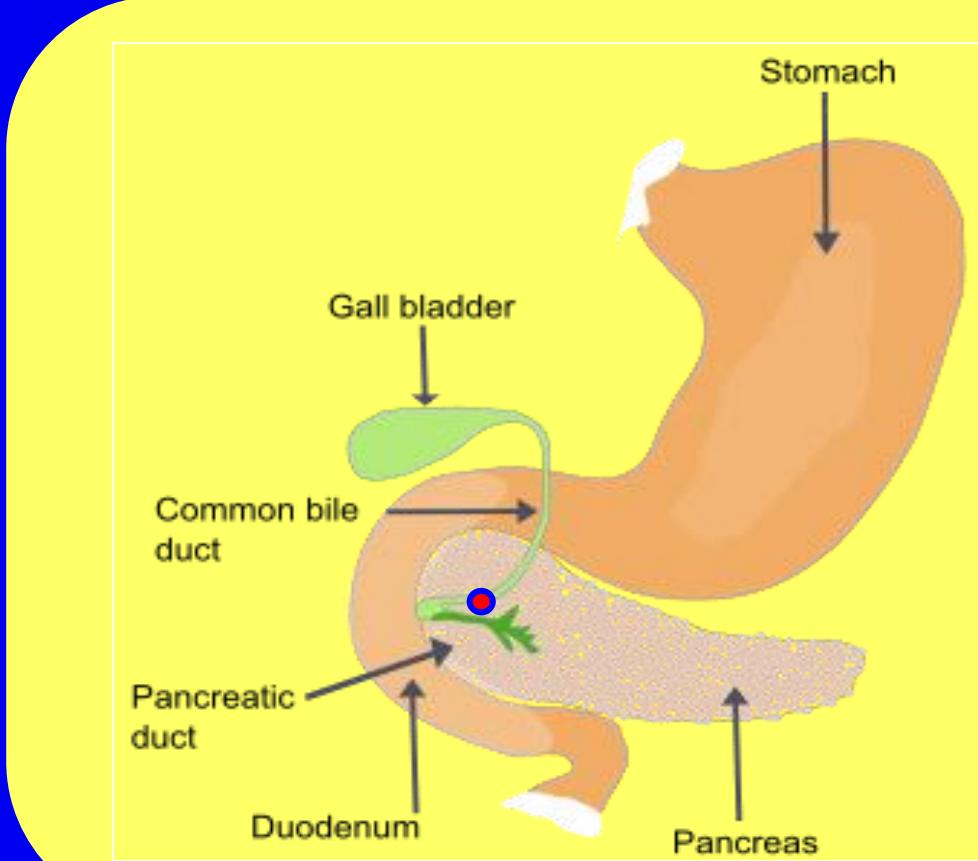
# Imaging tool for pancreas and prostate cancer biomarker development



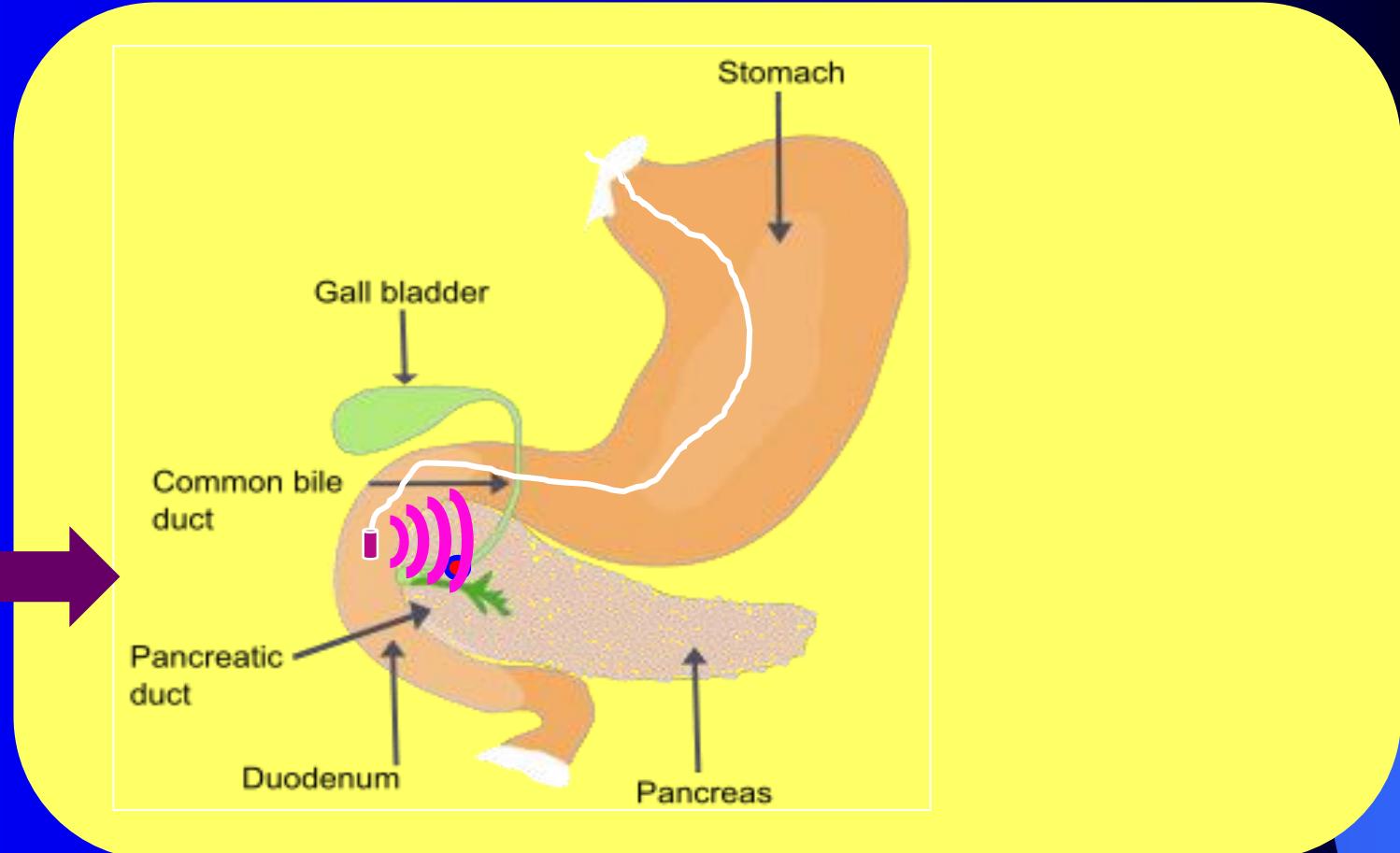
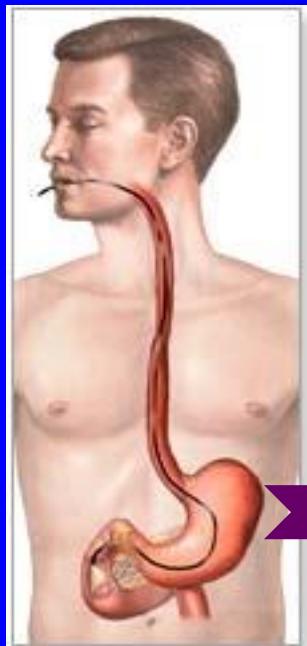
## *Objectives*

- Develop new biomarkers for pancreas and prostate cancer
  - Ex: mAb16D10 antibody for pancreas
  - Ex:  $^{68}\text{Ga}$  – PSMA for prostate
- Introduce PET as an endoscopic imaging tool
- Develop intra-operative interventional imaging techniques

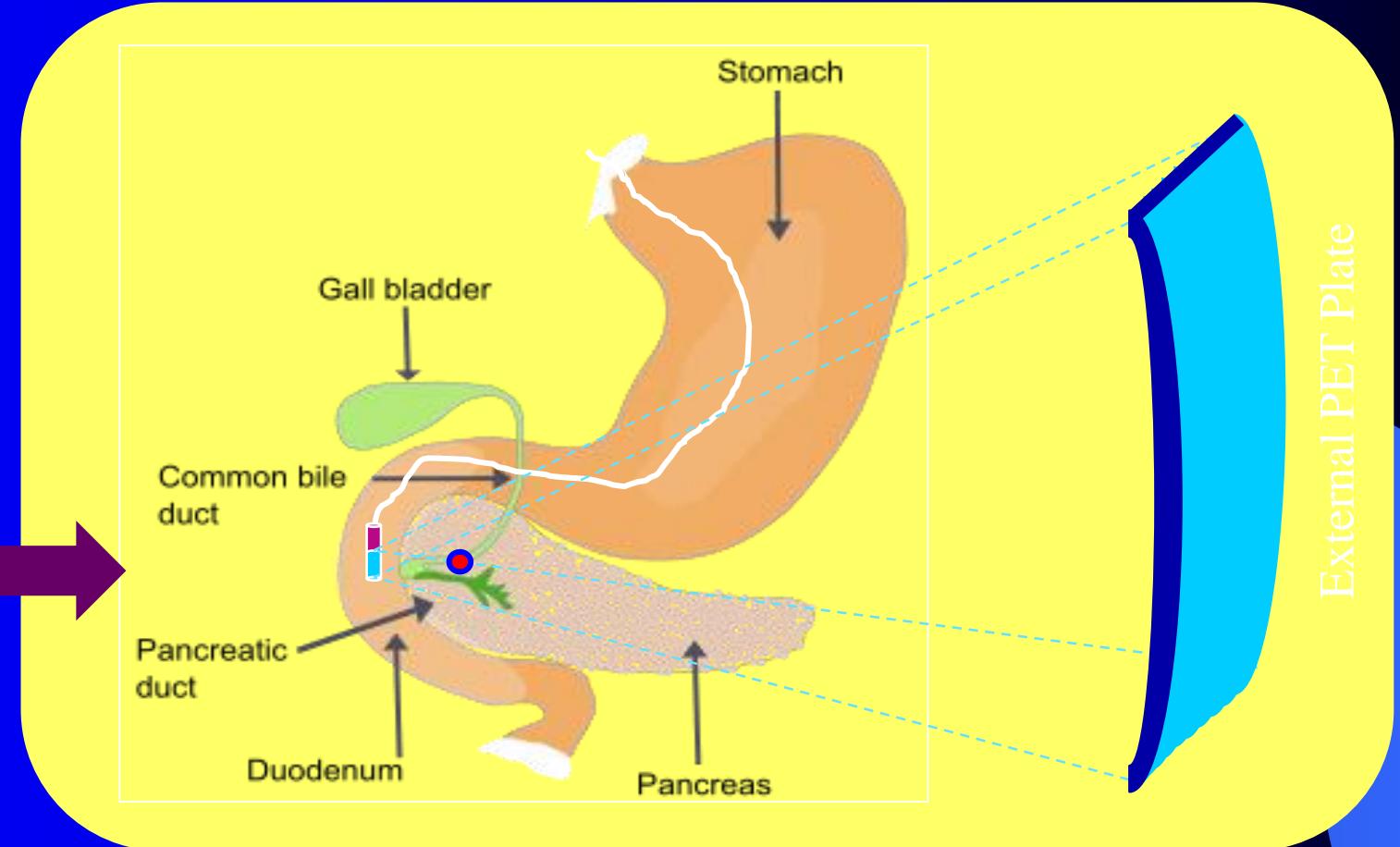
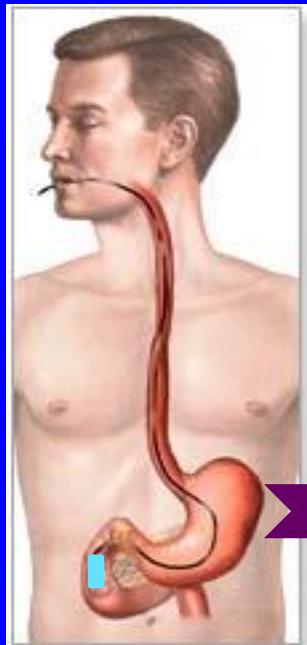
# EndoTOFPET-US: The Principle



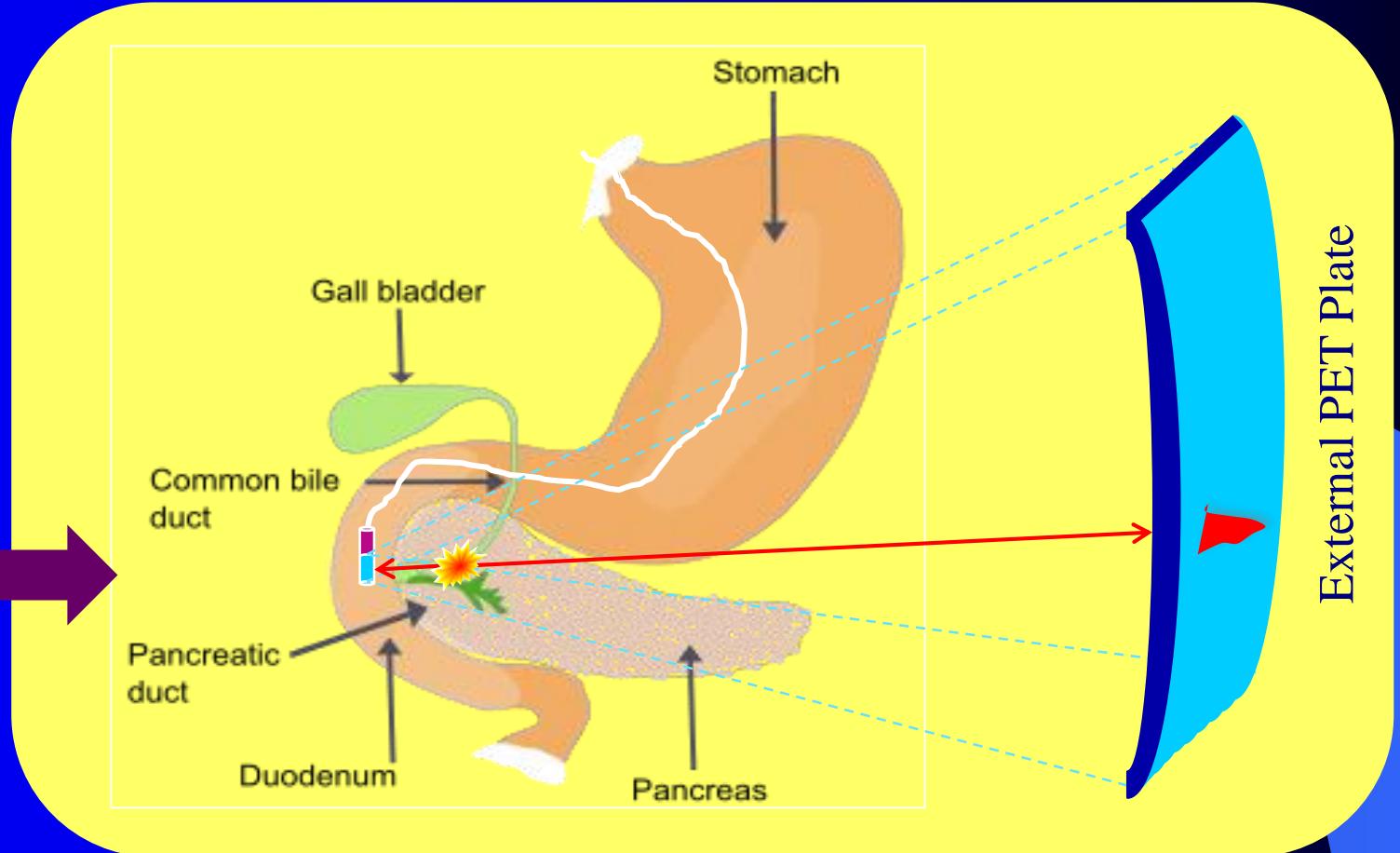
# EndoTOFPET-US: The Principle



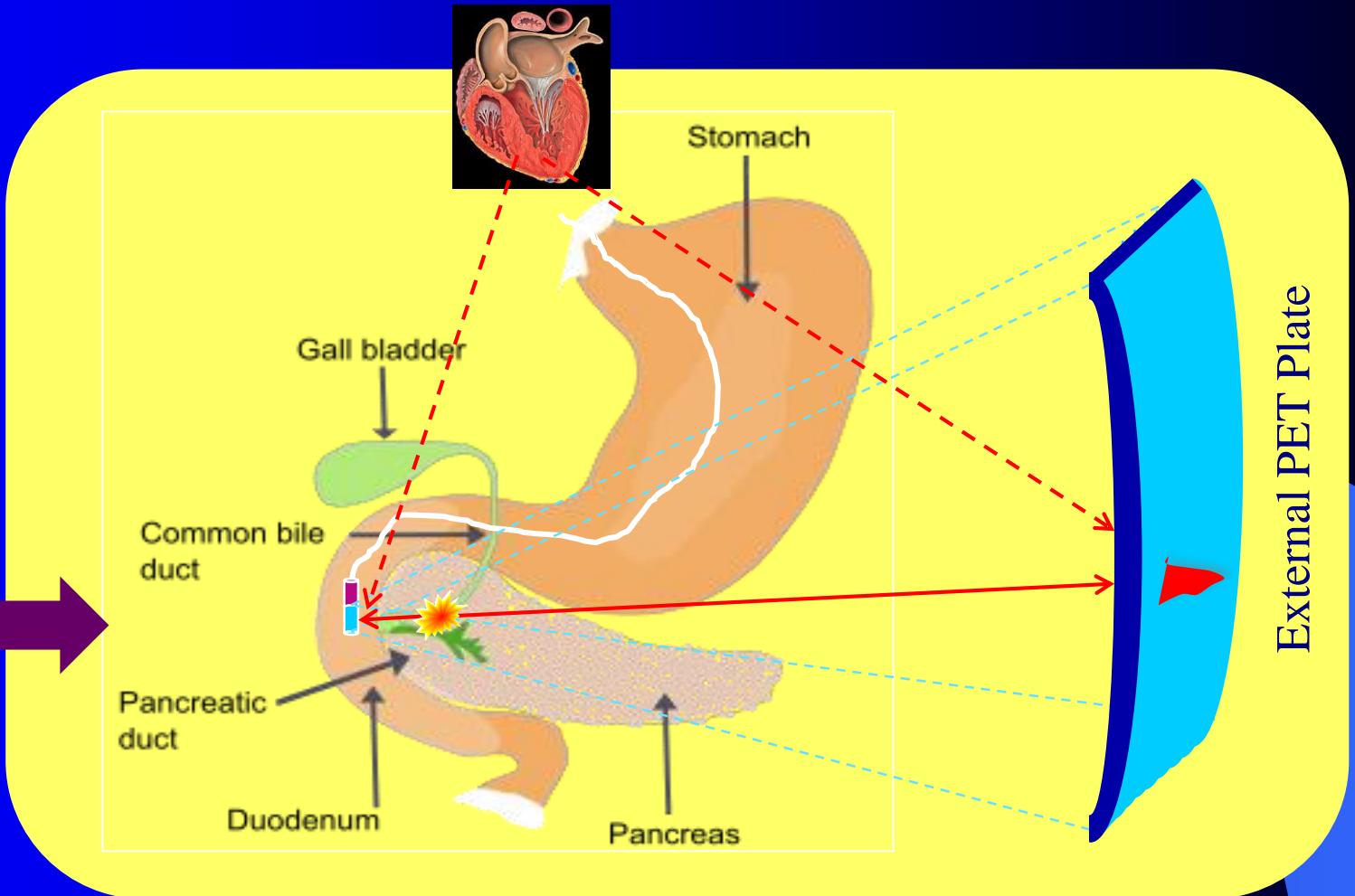
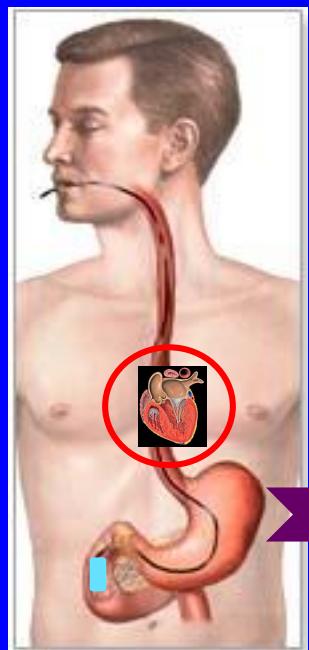
# EndoTOFPET-US: The Principle



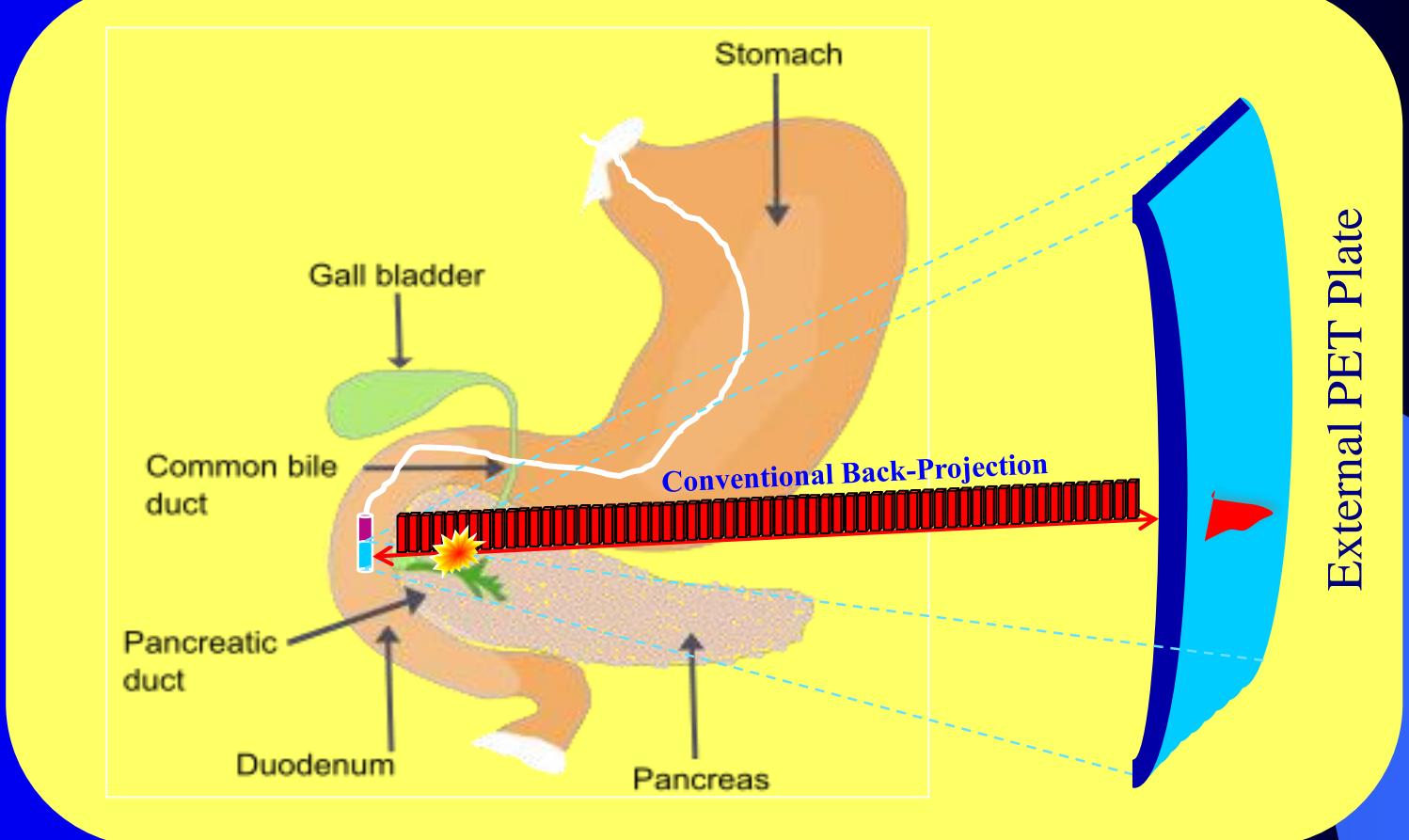
# EndoTOFPET-US: The Principle



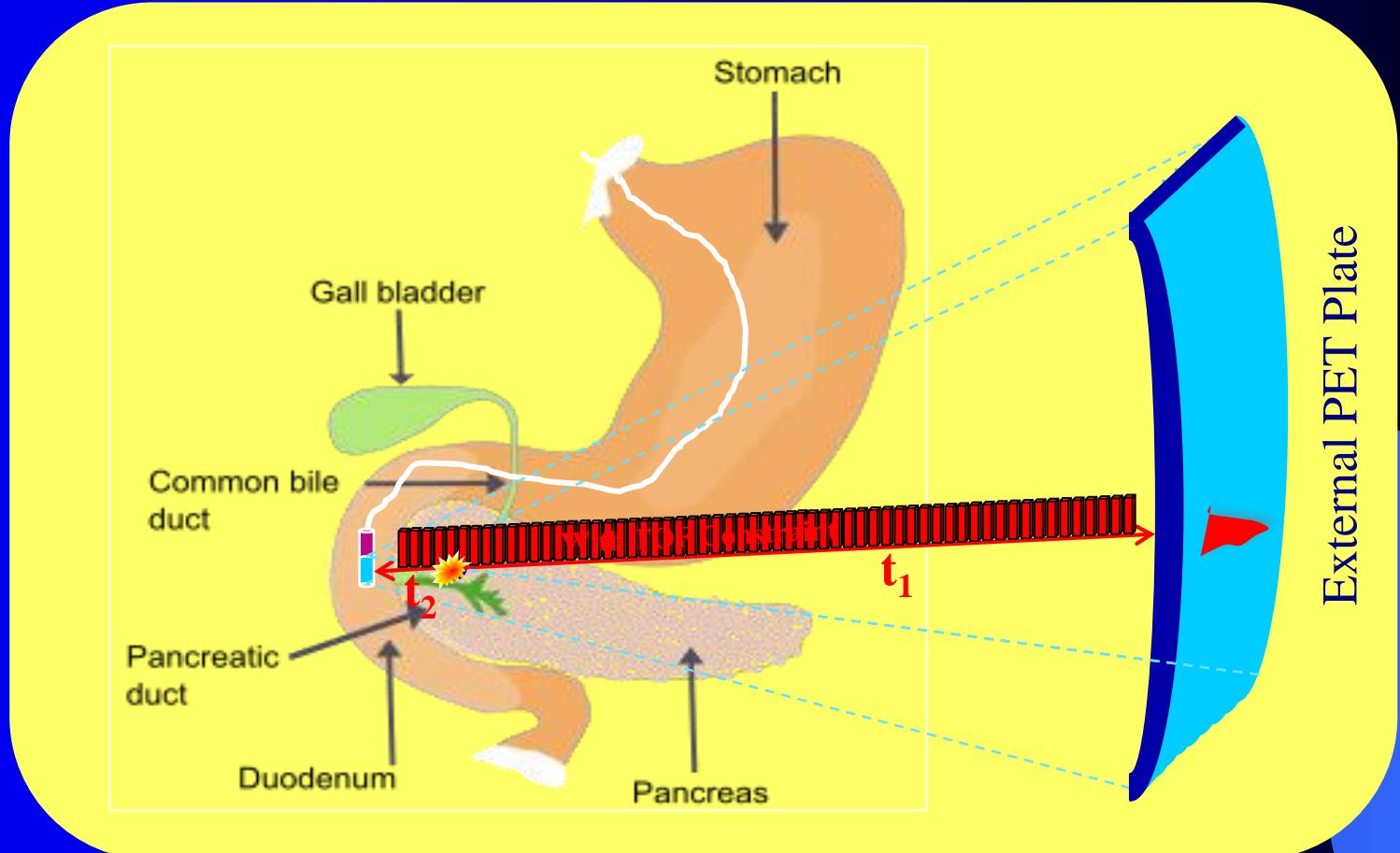
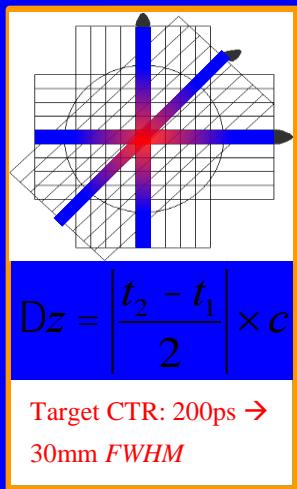
# EndoTOFPET-US: The Principle



# EndoTOFPET-US: The Principle

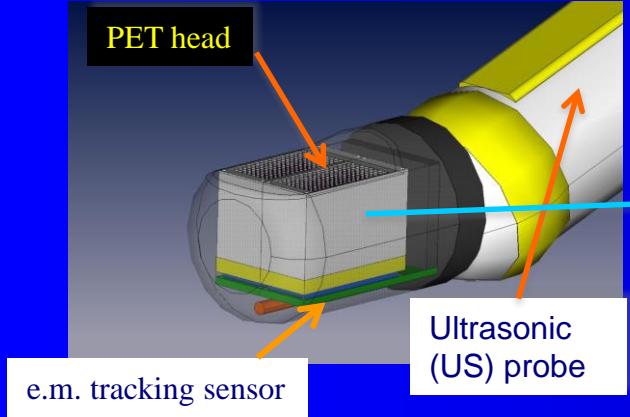


# EndoTOFPET-US: Why TOF?

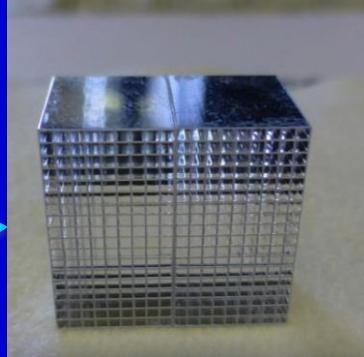


# Technical design

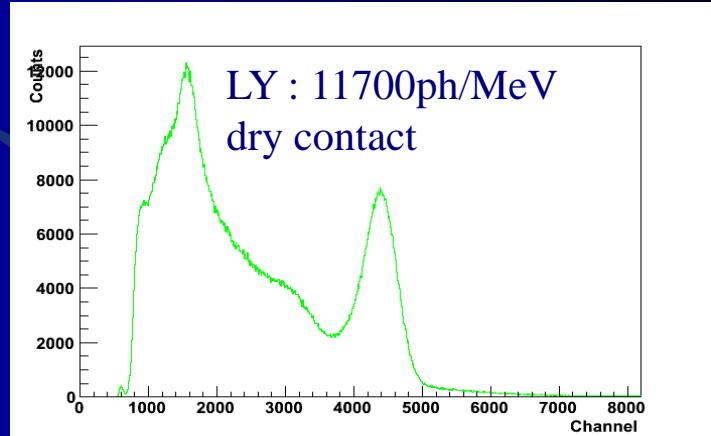
## Internal probe : 1 or 2 matrices of 9x18 LYSO pixels



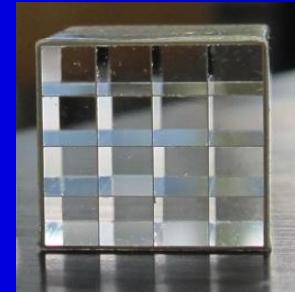
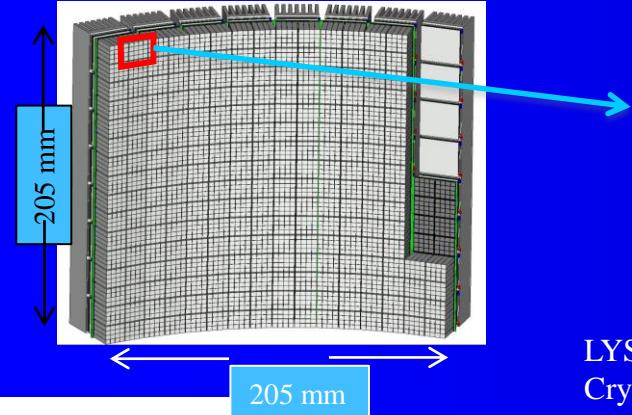
2 LYSO matrices from Proteus.  
 Crystal pitch: 800 $\mu$ m, length: 10mm  
 Coating: ESR reflector by 3M



Photopeak for entire matrix 9\*18 with dry contact

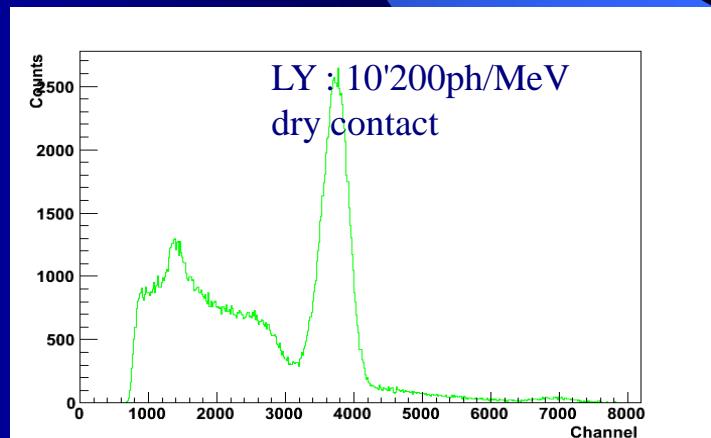


## External plate: 256 matrices of 4x4 LYSO pixels



LYSO matrix from CPI  
 Crystal pitch: 3.2mm, length: 15mm  
 Coating: ESR reflector by 3M

Photopeak for entire matrix 4\*4 with dry contact



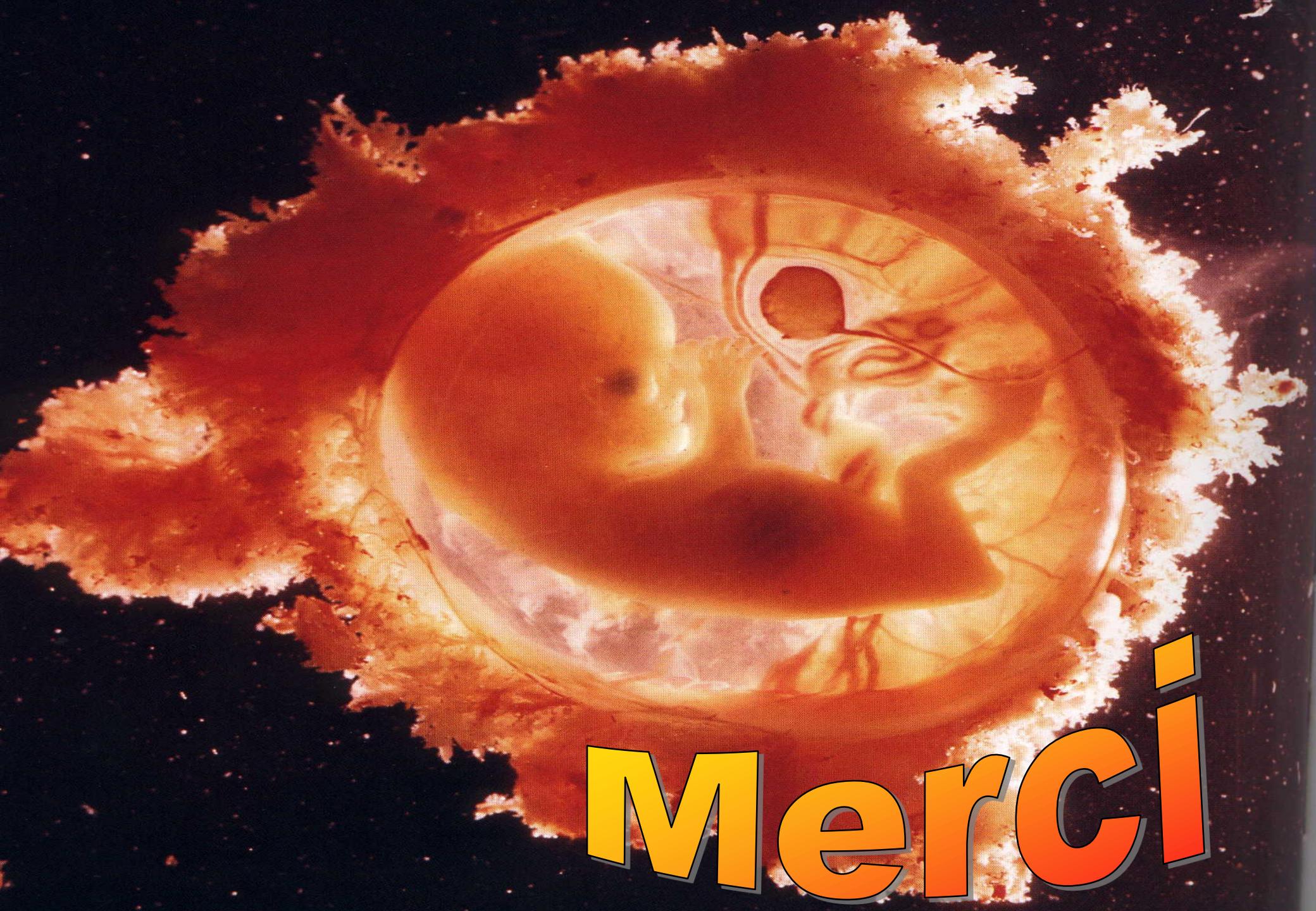
On both prototype matrices  
narrow photo-peak for the entire matrix  
 --> uniform LY among pixels

# Molecular Imaging in Medicine & Biology

- ◆ Molecular Imaging to answer challenge of modern biology
  - Access real time genomics through *in vivo* imaging of molecular process
  - Detect early transformations in a cell, which may lead to pathology (precancerous activity)
  - Early detection, prognosis, treatment selection, response to therapy
  - Identify molecular pathways from gene to disease (genomics, proteomics)
    - » Novel molecular targets
    - » Specific genetic pathways
    - » Signal transduction
    - » Cell cycle alteration
    - » Angiogenesis
    - » Apoptosis

**Requires specific effort on imaging instrumentation  
Sensitivity, Spatial and Temporal resolution**

**Requires targeting the cellular activity  
with specific contrast agents**



Merci