Physique

et

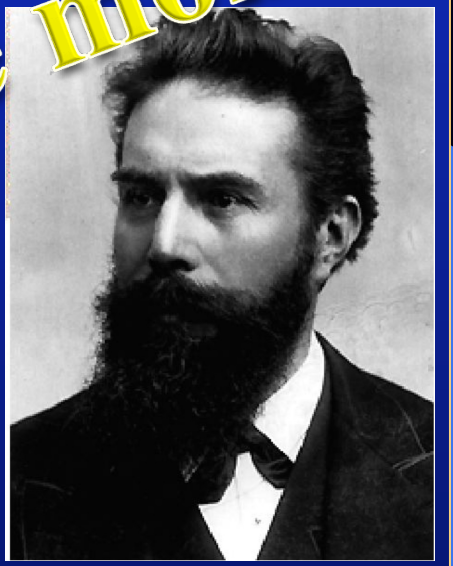
Imagerie Médicale

Paul Lecoq
CERN, Genève

La découverte des Rayons-X

- Le 8 November 1895 Röntgen découvre les Rayons X
- Le 22 November 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 **1er prix Nobel de physique** en 1901

Premières applications dans la thérapie du cancer

Basic concept

Local control of the tumour

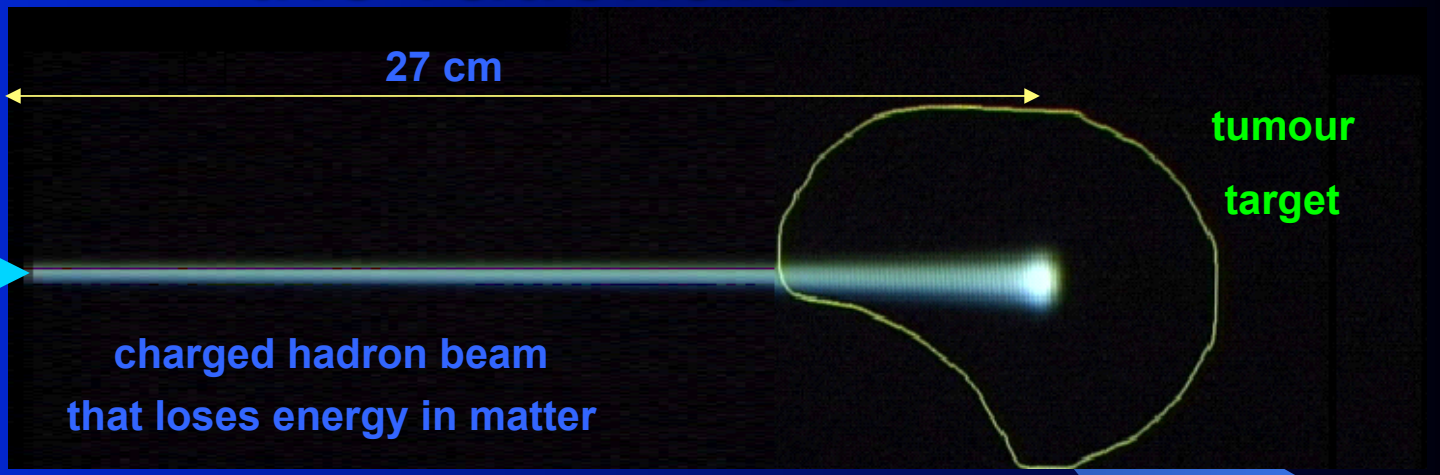
1908 : first attempts of skin cancer radiation therapy in France ("*Curietherapy*")

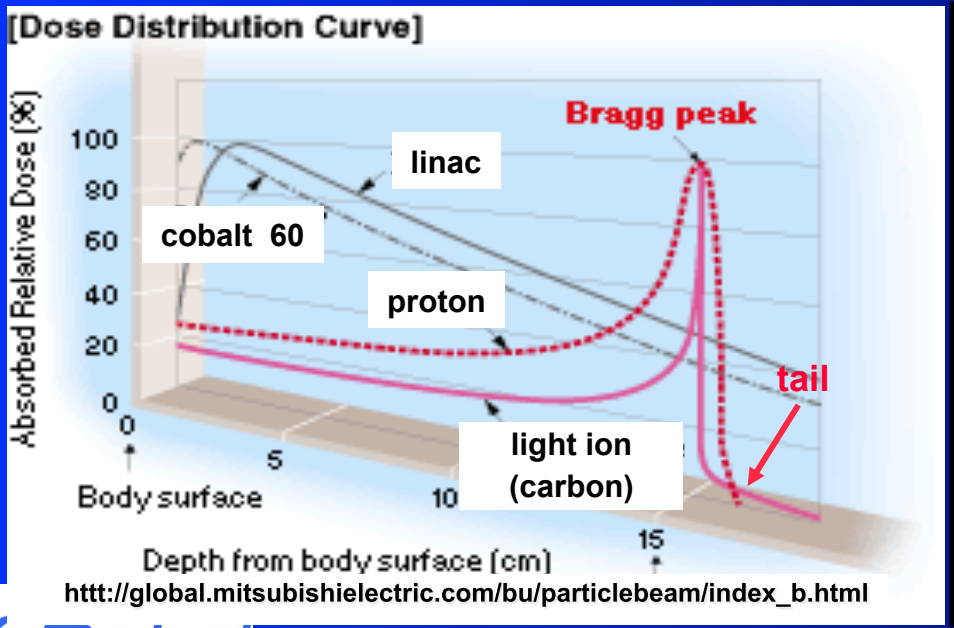
Hadrontherapy accelerators the rationale

200 MeV - 1 nA protons

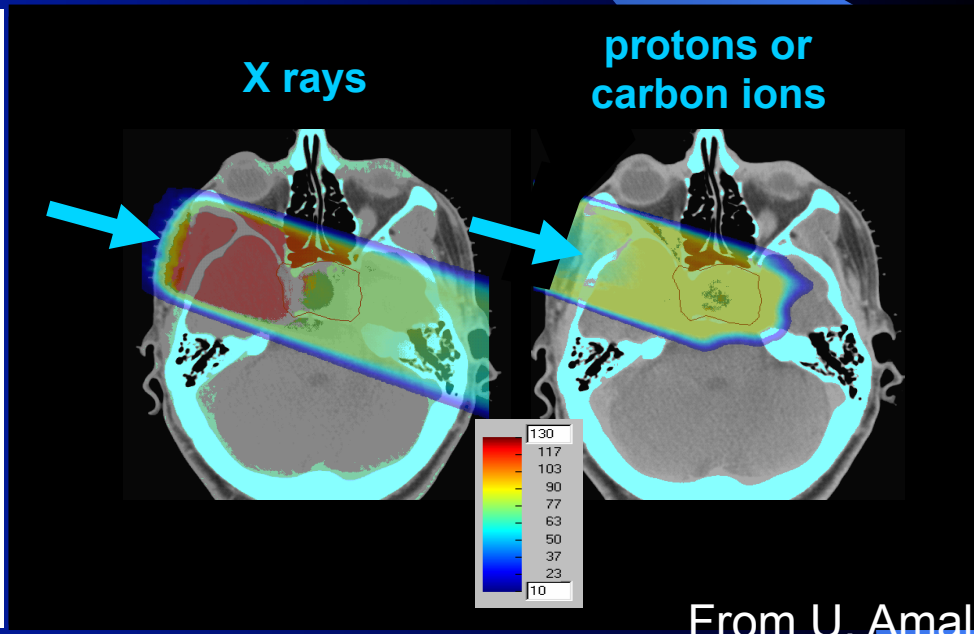
4800 MeV – 0.1 nA carbon ions

which can control radioresistant tumours





htt://global.mitsubishielectric.com/bu/particlebeam/index_b.html



From U. Amaldi

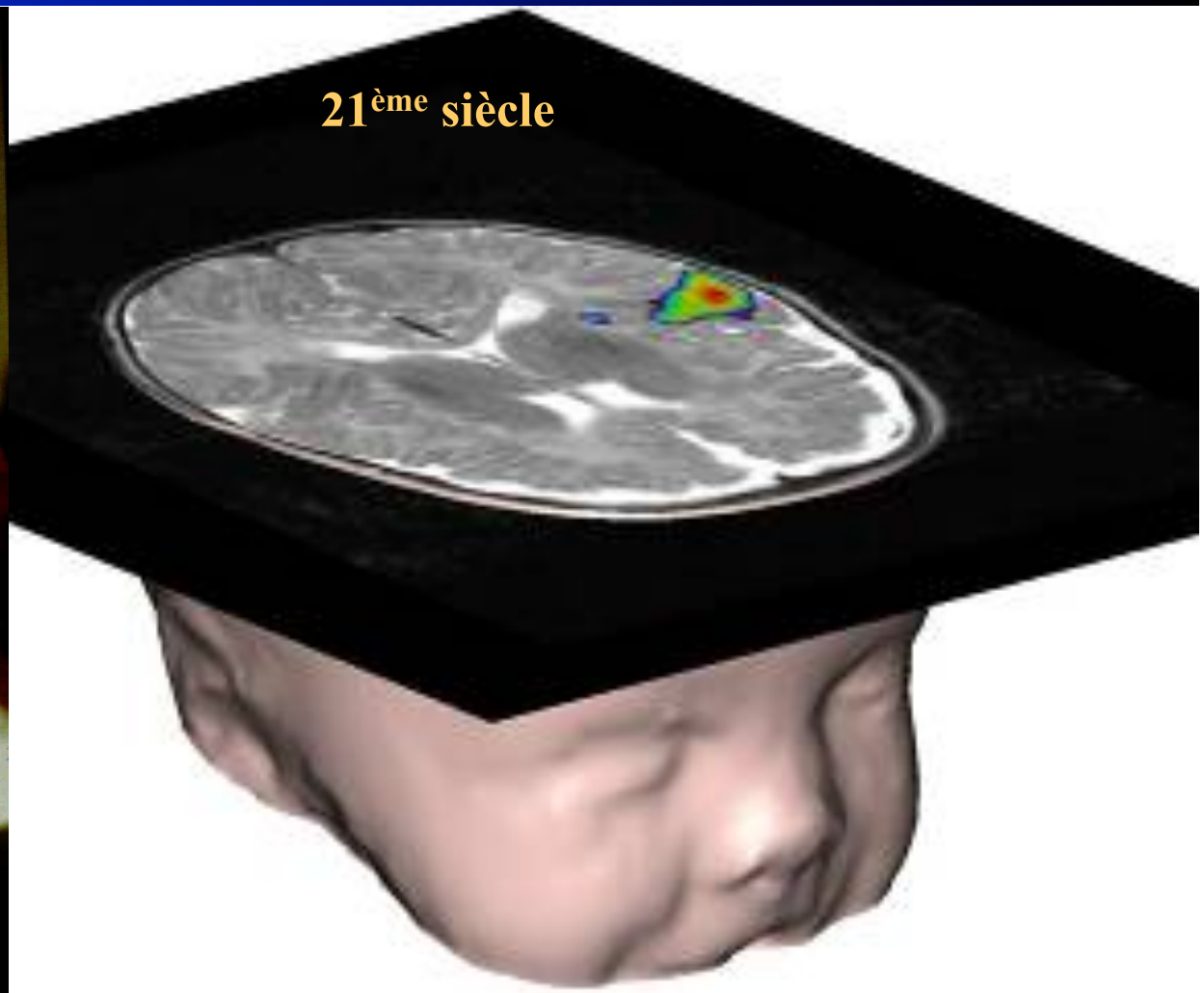
Summary of accelerators running in the world

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

9000

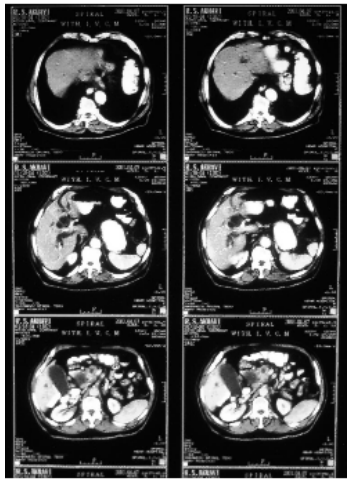
(*) W. Maciszewski and W. Scharf: Int. J. of Radiation Oncology, 2004

Petite histoire résumée de l'imagerie in-vivo



De moins en moins invasive

Imaging Modalities

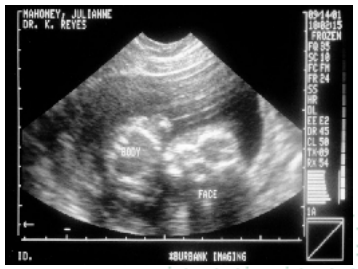


CT

A

Tissue Density, Z
20-50 µm

Ultrasound



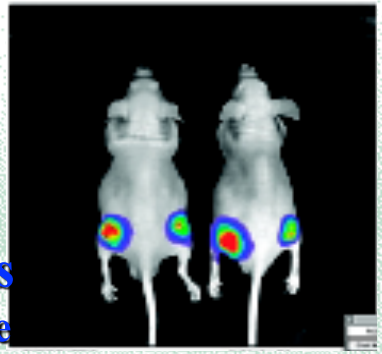
A F

Structure
0.1 mm
Doppler

Optical
(Bioluminescence, fluorescence)

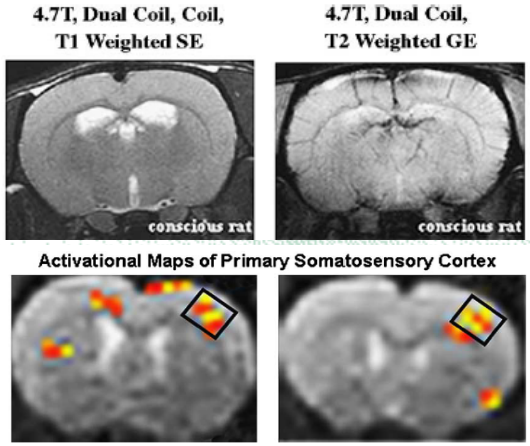
A M

Topography
µm to mm
~10^3 cells
≠ quantitative



Photons involved

MRI



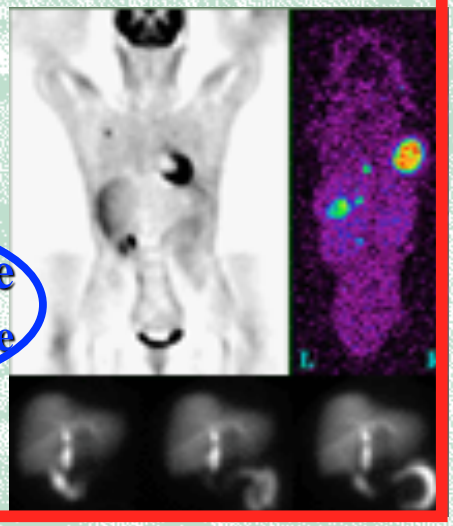
A F M

H Concentration
0.1 mm
BOLD, DCE
β-galactocidase
0.1 µmole H / µmole ^{31}P

PET/SPECT

F M

Radiotracer
~1-2 mm
<10^{-12} mole
= quantitative



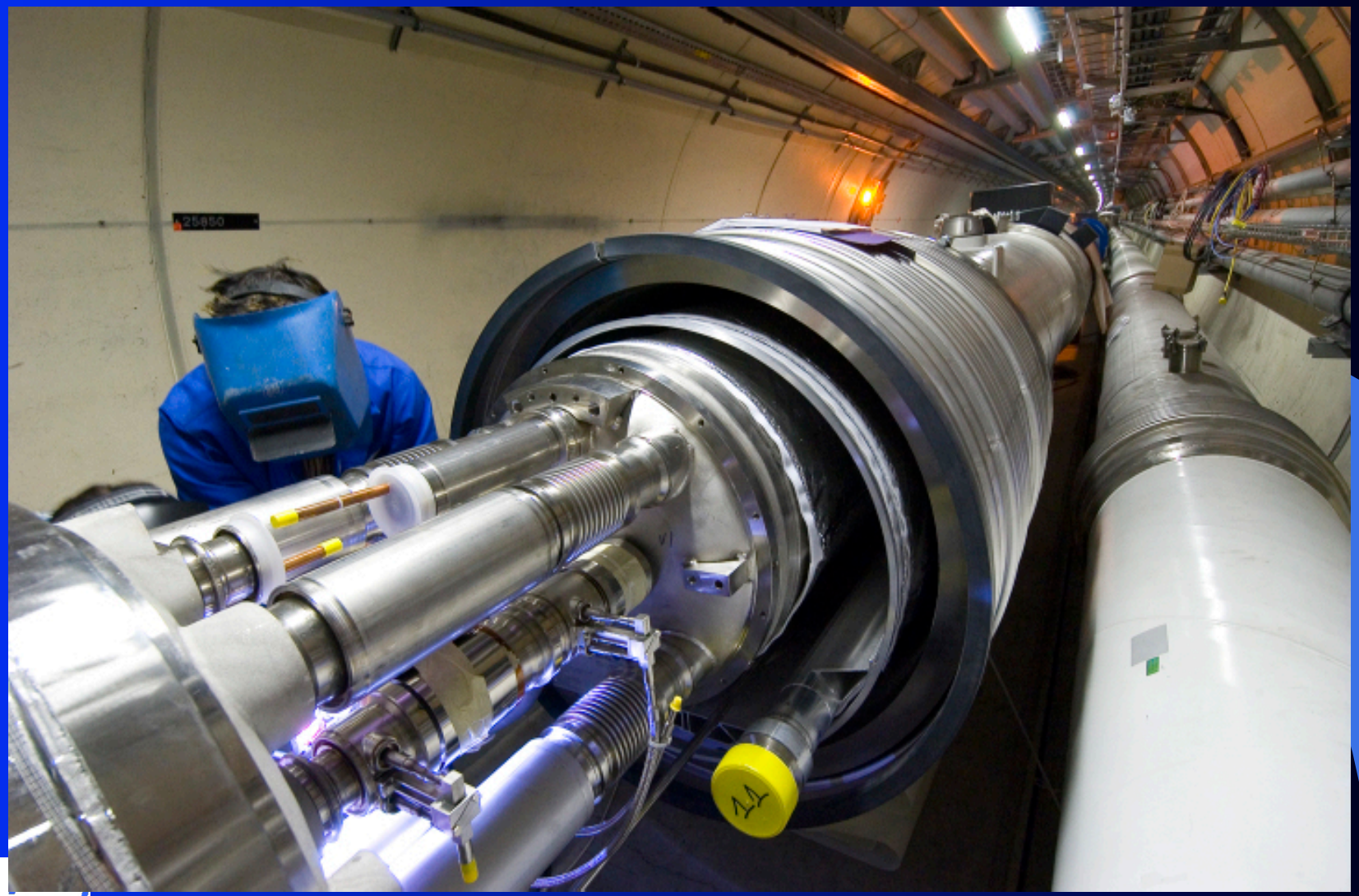
L'imagerie pour une meilleure prise en charge du patient

Recueillir une information détaillée de chaque individu pour:

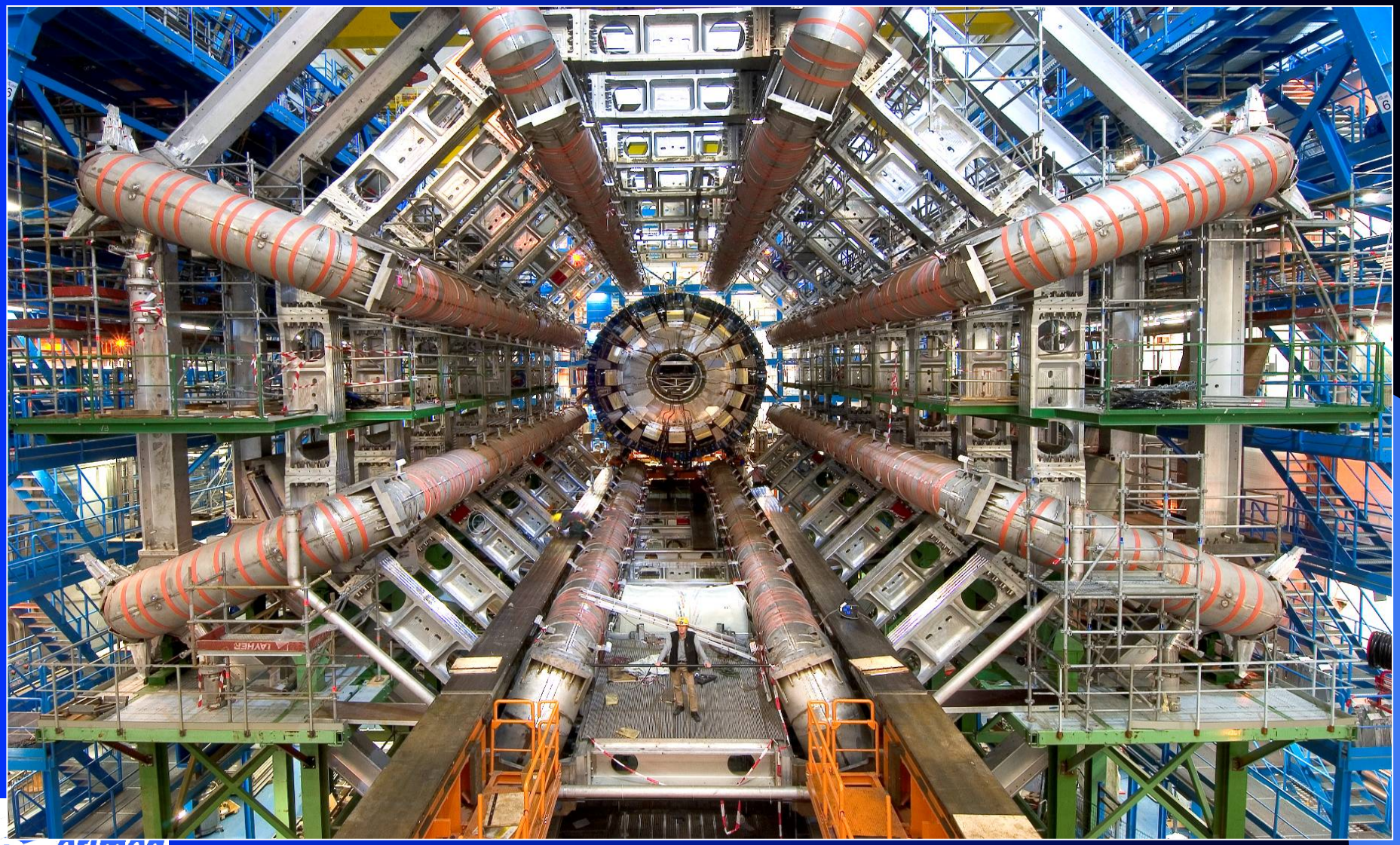
- Diagnostiquer la maladie à un stade précoce
- Déterminer les paramètres de la maladie, comme son agressivité, son potentiel métastasique
- Optimiser l'action thérapeutique en fonction du génotype du patient
- Evaluer instantanément l'efficacité du traitement

Implique une nouvelle génération de systèmes d'imagerie

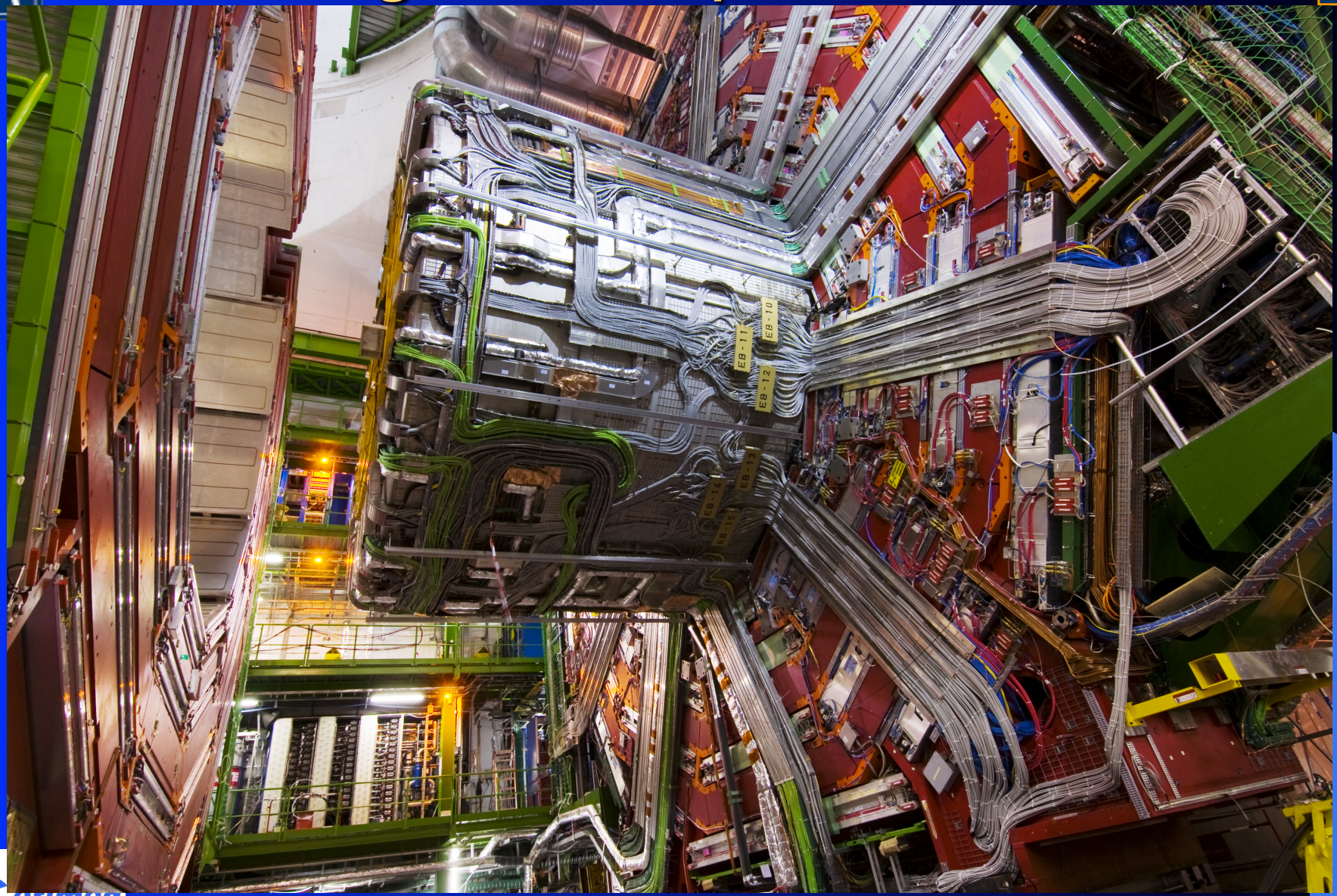
LHC - Installation des aimants supraconducteurs (27km)



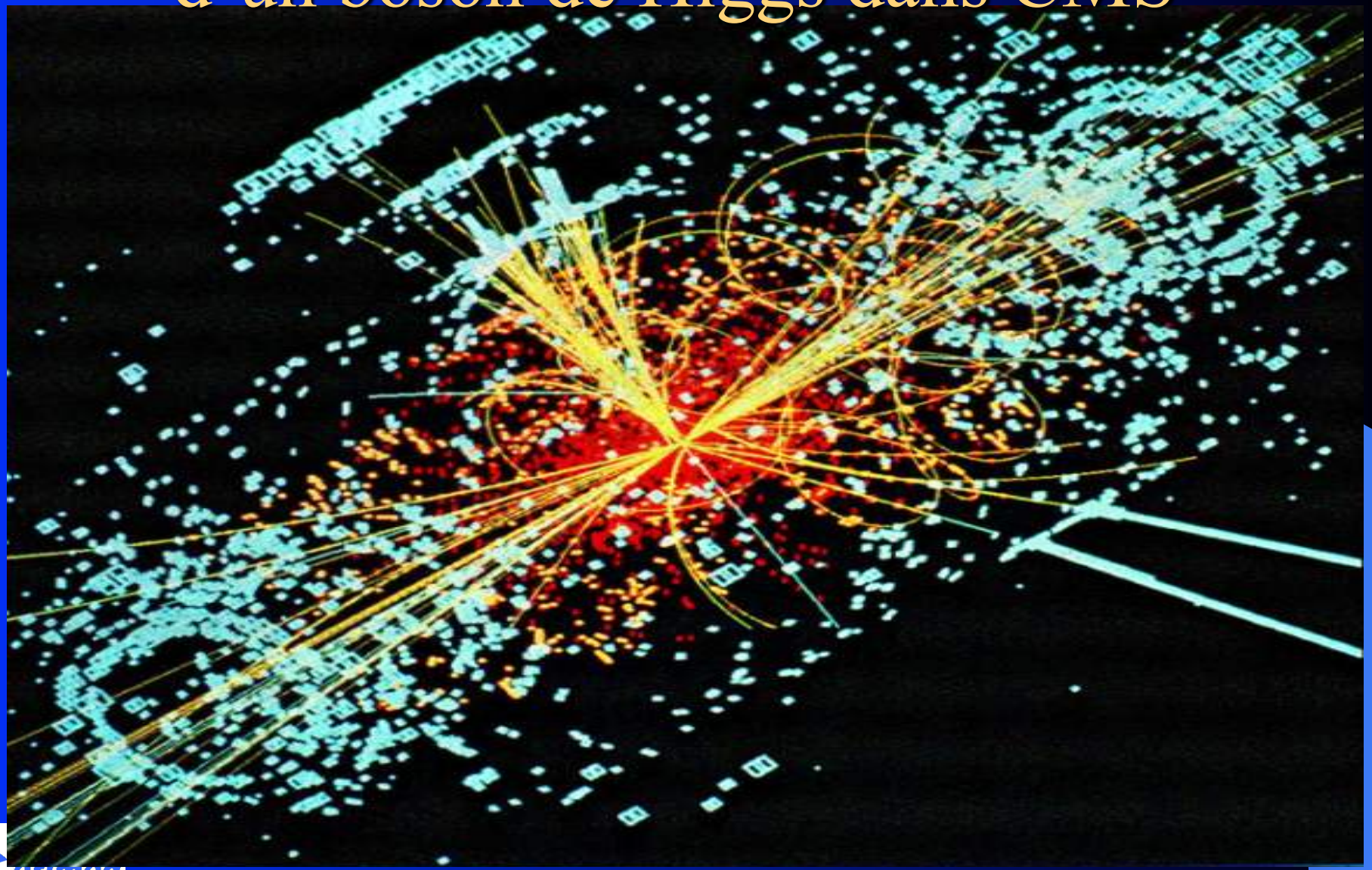
L'aimant toroïdal d'Atlas



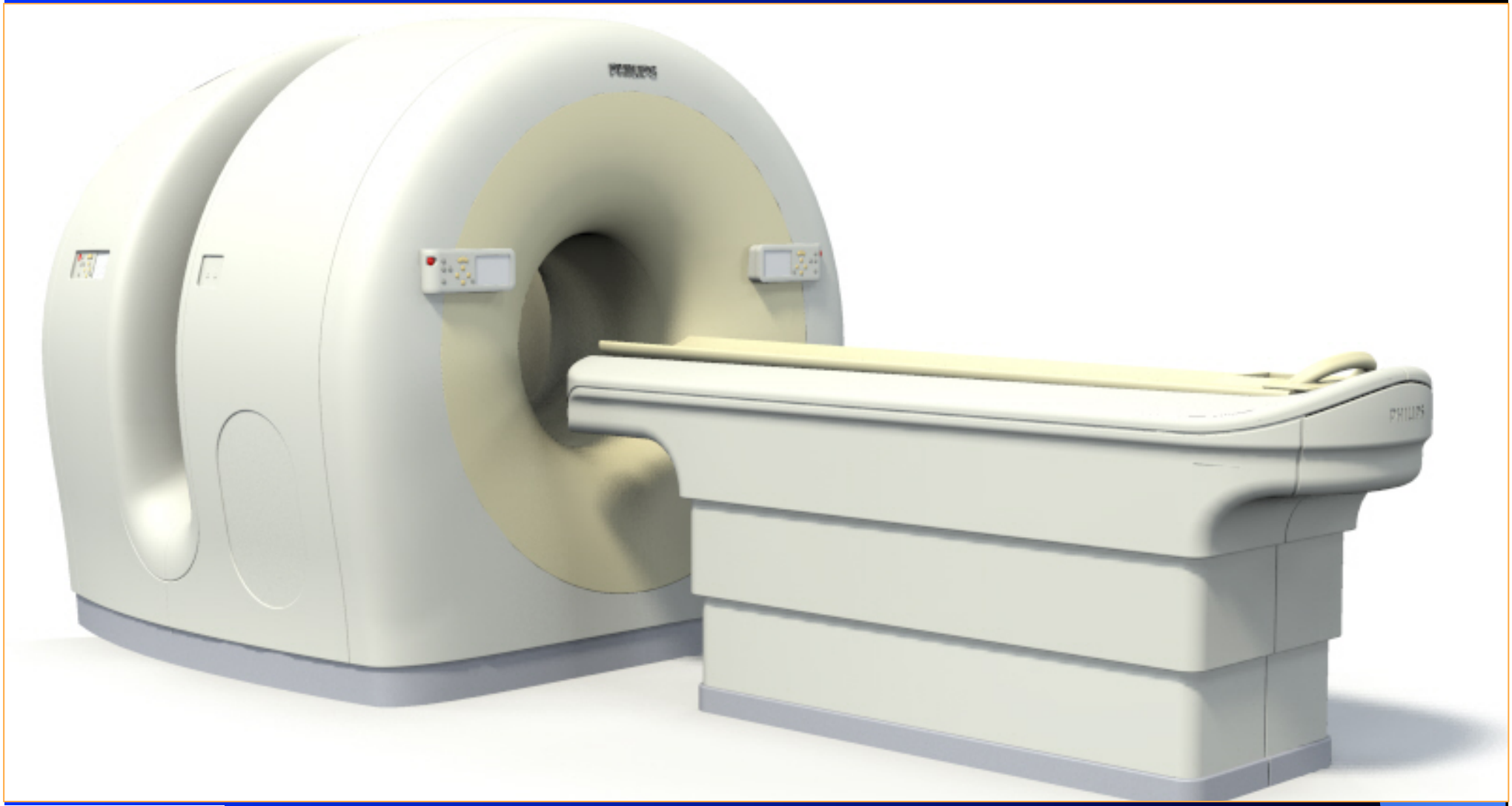
Montage de l'expérience CMS



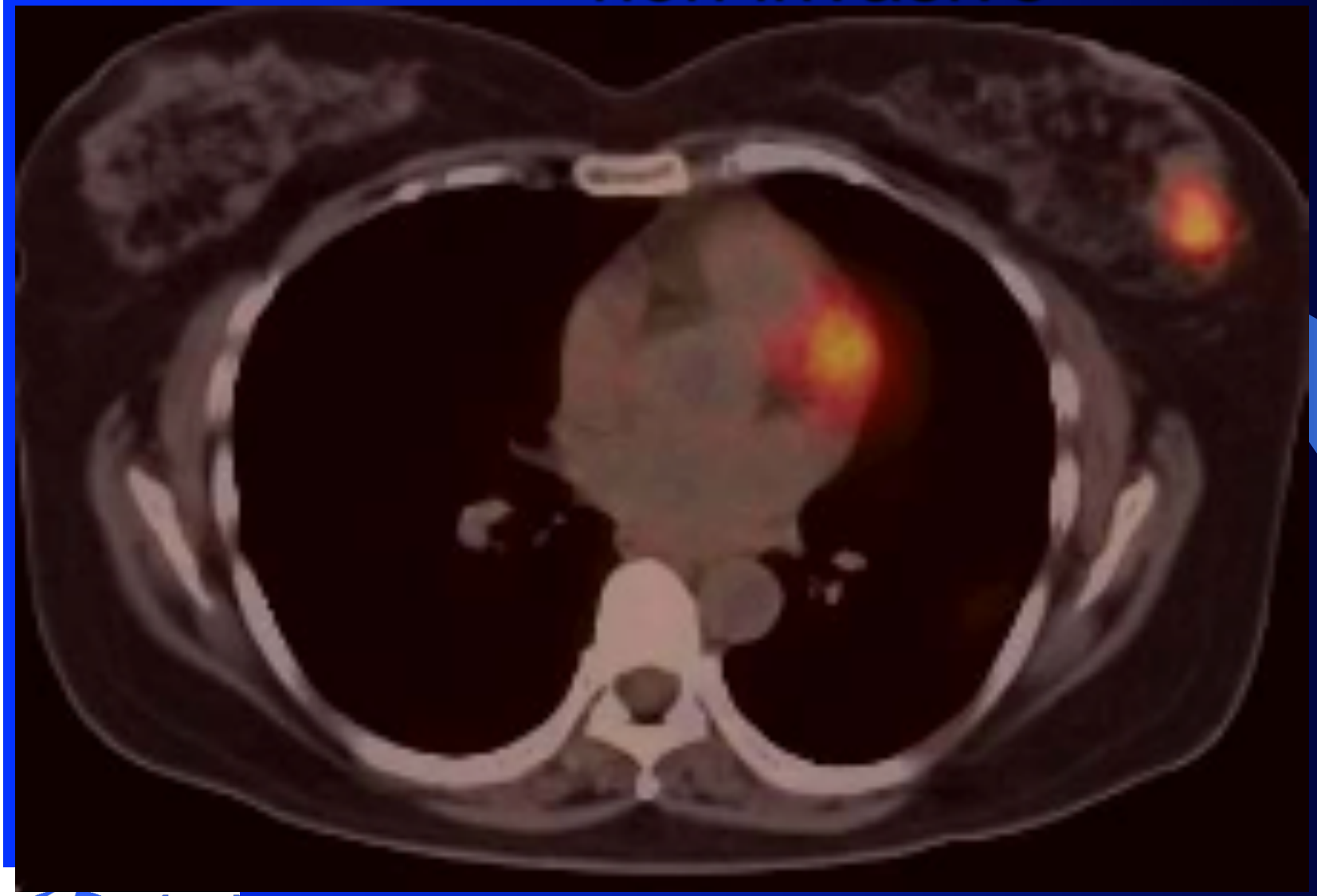
Simulation de la désintégration d'un boson de Higgs dans CMS



Scanner TEP/CT



Imagerie anatomo-fonctionnelle non invasive

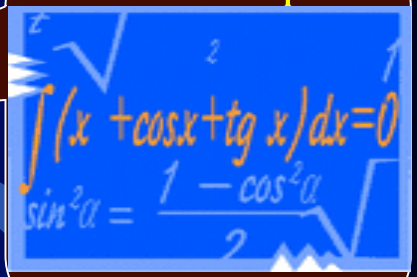


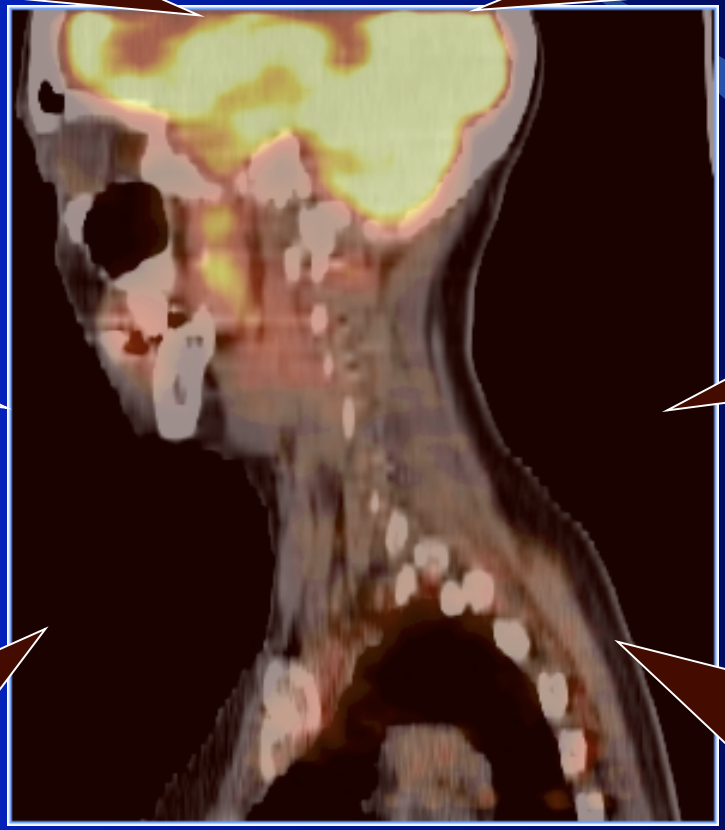
Patiente traitée pour un cancer du colon révélant à l'examen un cancer du sein additionnel

L'imagerie médicale: une approche pluridisciplinaire

Physique

Mathematiques





Médecine

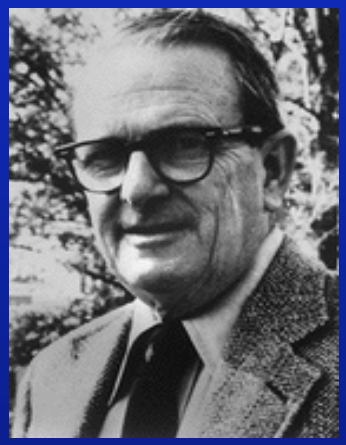
Chimie

Biologie

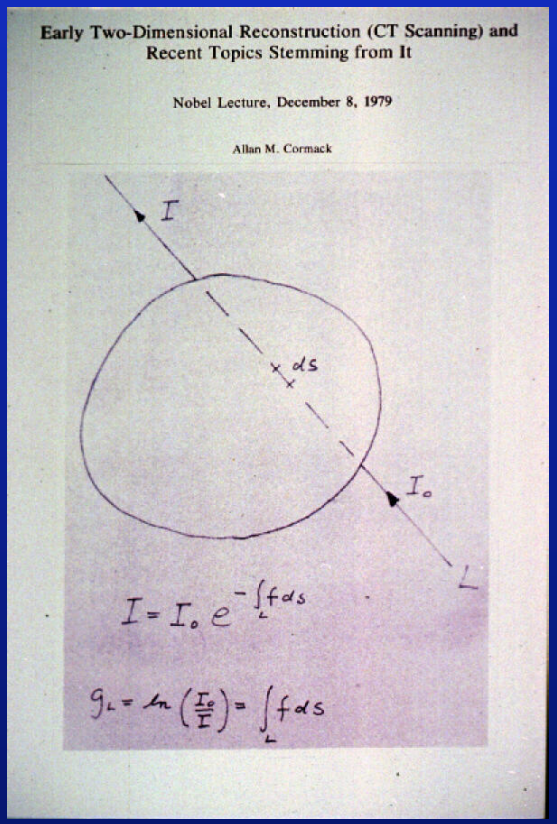
Informatique

CAT Scanner
Le principe de la tomographie

Prix Nobel de Physiologie et Médecine 1979

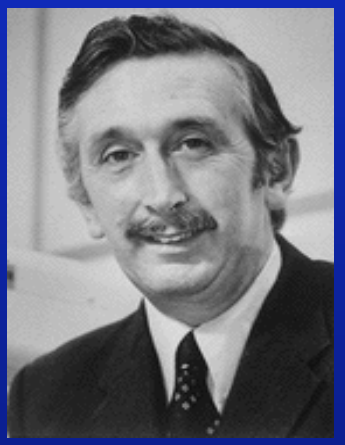


Allan MacLeod **Cormack**
Physicien Nucléaire
Cape Town
Harvard University
Tufts University


Early Two-Dimensional Reconstruction (CT Scanning) and Recent Topics Stemming from It

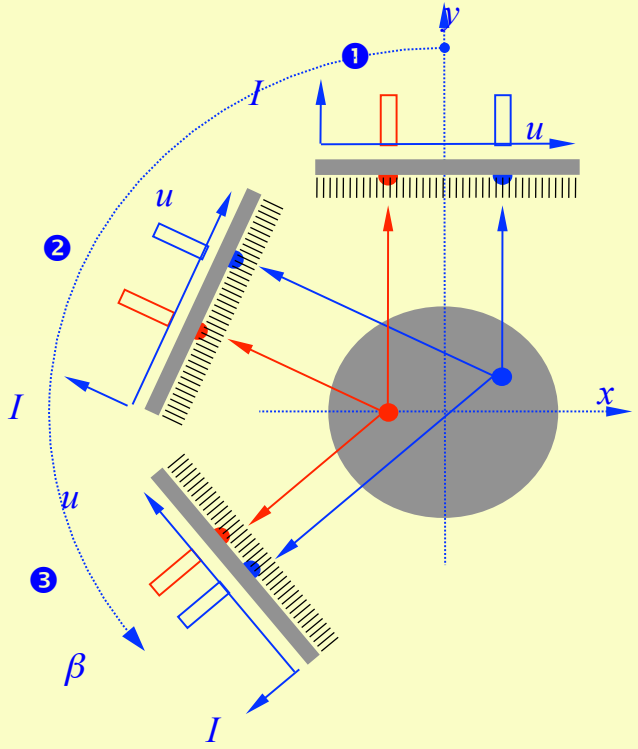
Nobel Lecture, December 8, 1979

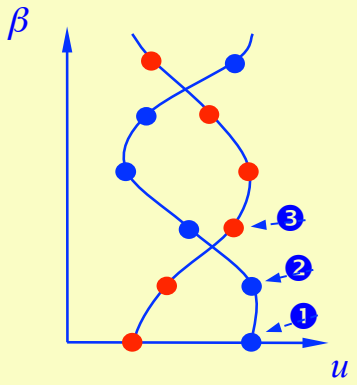
Allan M. Cormack

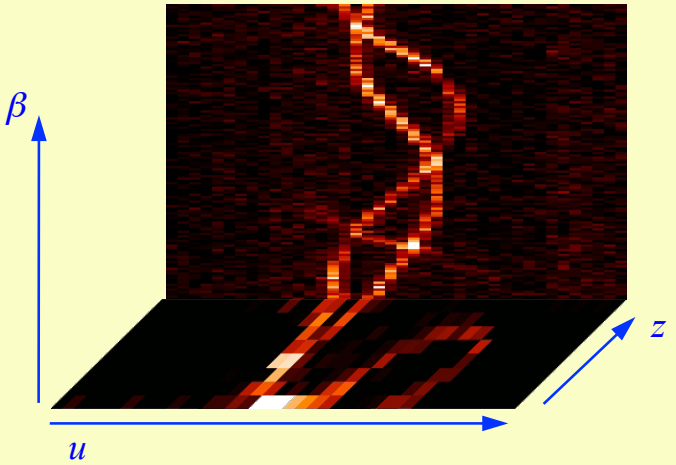


Sir Godfrey N. **Hounsfield**
Ingénieur électricien anglais
EMI Research

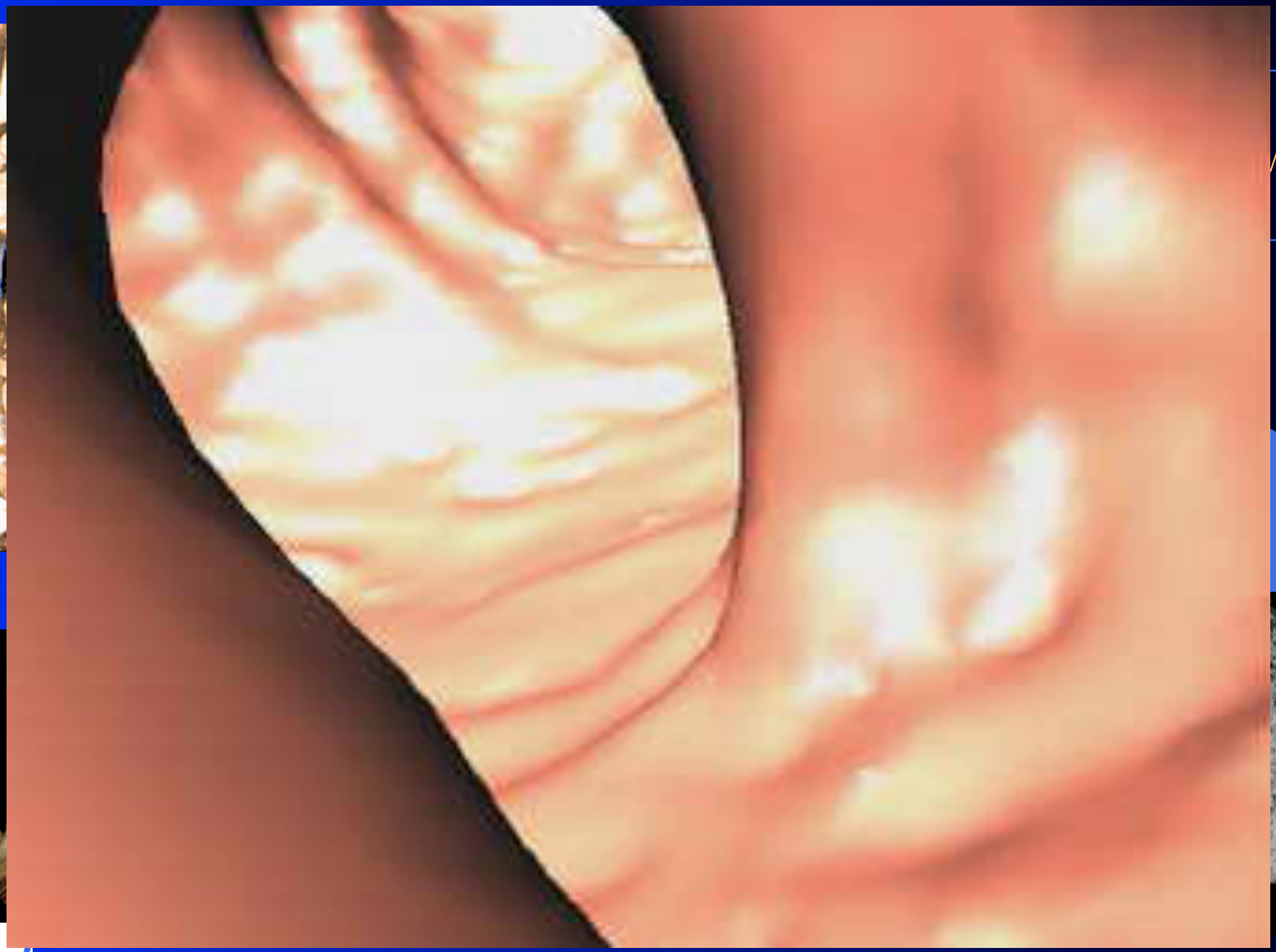
Principle of CT







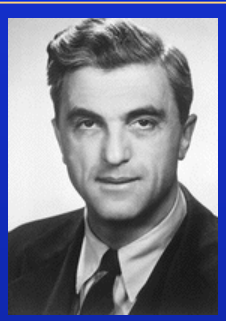
Volumetric CT



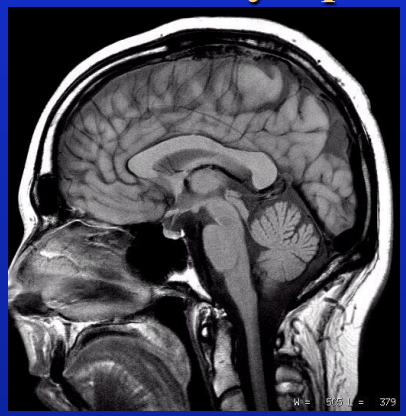
/sec)

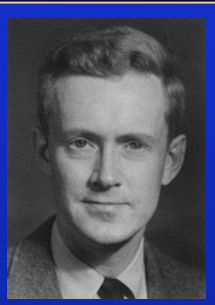
IRM, imagerie par résonance magnétique

Prix Nobel de Physique 1952



Felix Bloch
Physicien Stanford

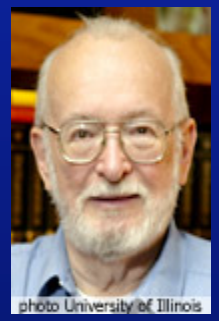




Edward M. Purcell
Physicien Harvard

Prix Nobel de Physiologie et Médecine 2003

Sir Peter **Mansfield**
Physicien Nottingham

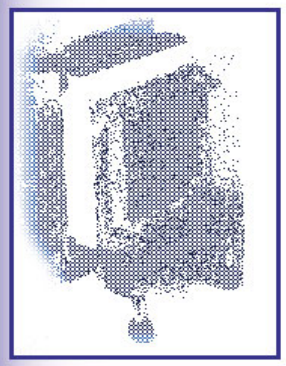


Paul C. **Lauterbur**
Chimiste Uni. Illinois

Un peu d'histoire

1977

when PET started at CERN

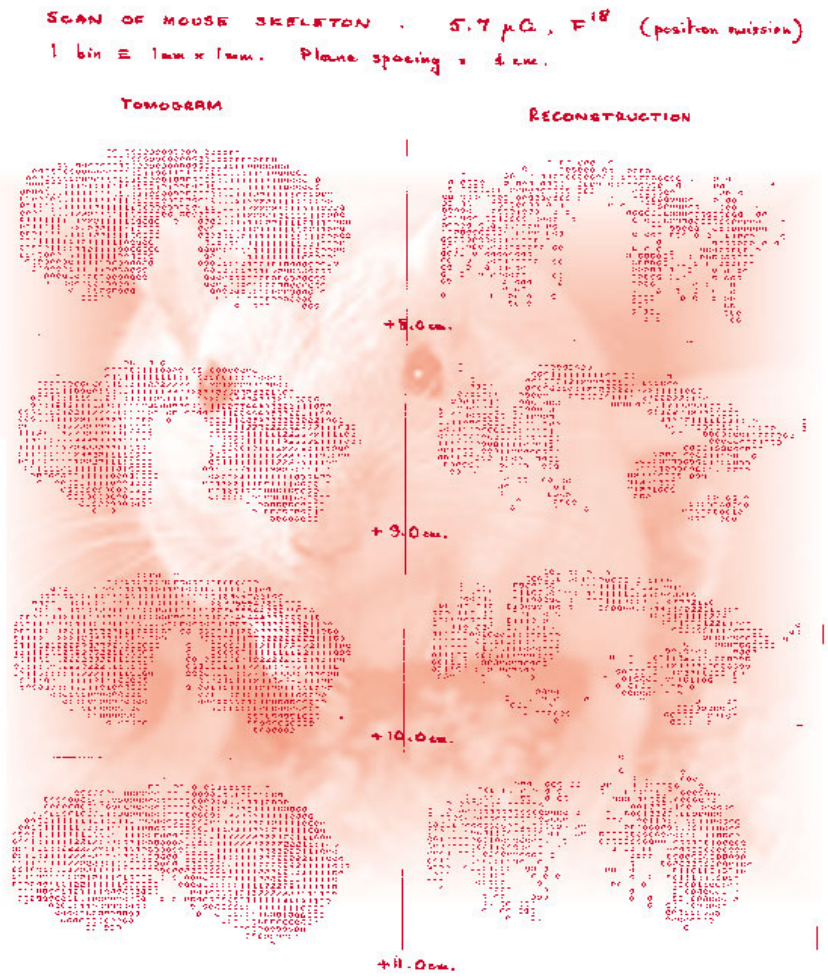


(Jeavons, Townsend et al.)

Spatial resolution 2.4 mm FWHM
Maximum data rate: 3000 c.p.s

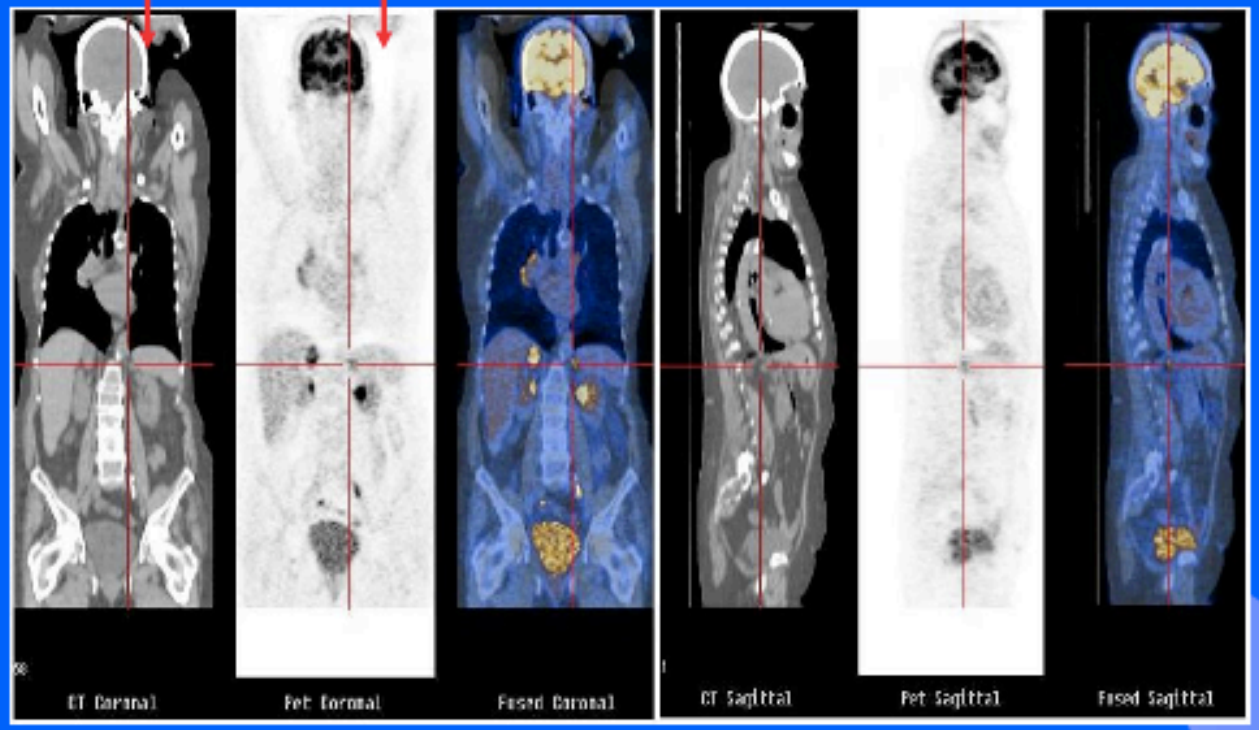
Sensitivity: 25 c.p.s/ μCi

1 μCi=3.7 10⁴Bq



CERN Technology Transfer http://cern.ch/TTdb

Combiner les informations anatomique et fonctionnelle



David Townsend

CERN: 1970-78

Université de Genève

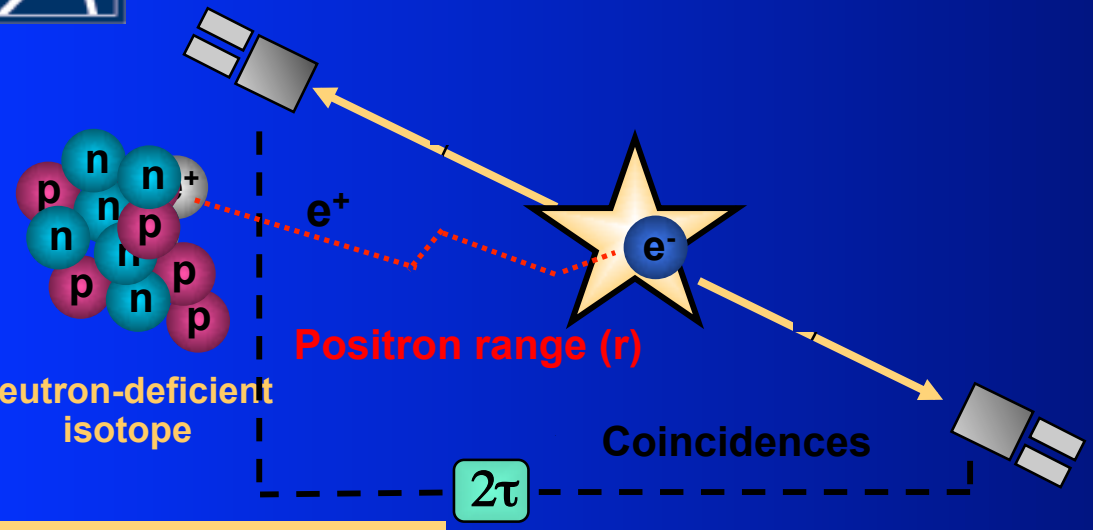
UPSM Pittsburgh

and

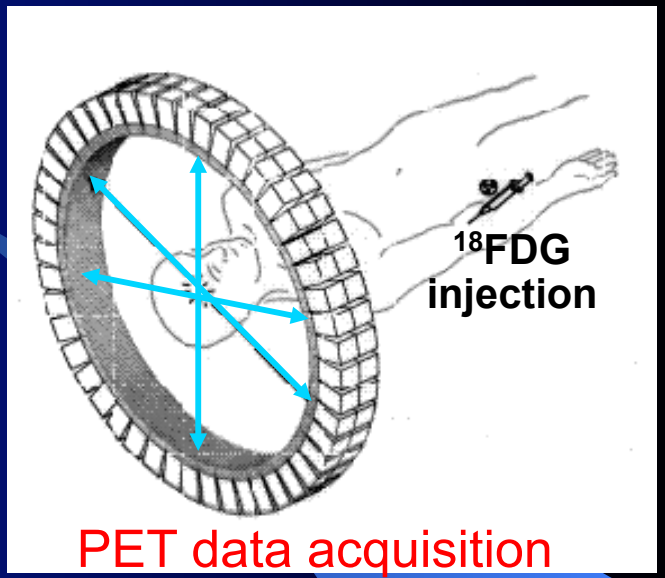
Ronald Nutt

(CTS – CTI)

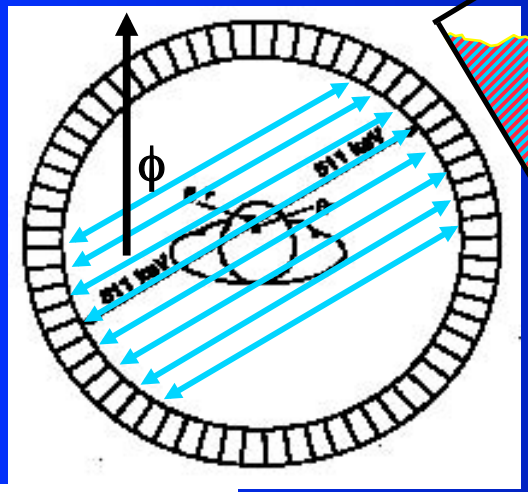
PET Principle



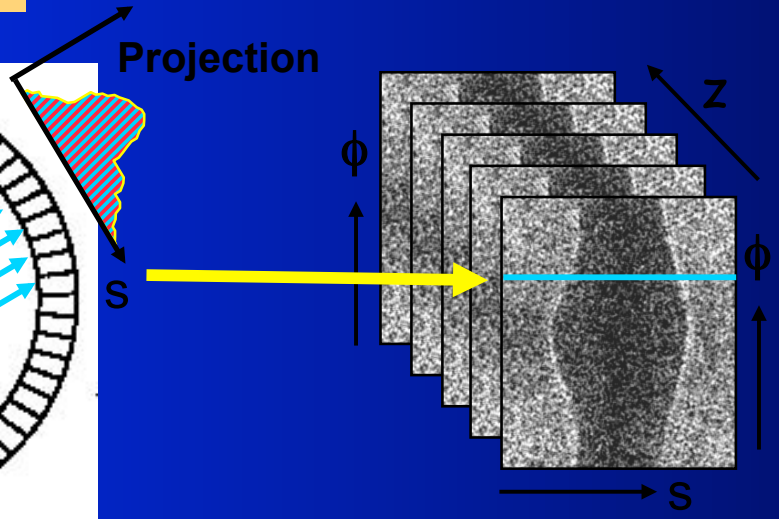
(6p; 5n)➔(5p; 6n)



PET data acquisition



Parallel projections



PET data (sinograms)

Reconstruction

PET images

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

Cahier des charges pour la physique

1. **Cristaux**
   - Densité élevée (> 6 g/cm^3)
   - Emission rapide (< 100 ns), spectre visible
   - Emission lumineuse modérée à élevée
   - Excellente résistance 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**
   - Sytèmes compacts avec un très grand nombre de canaux (> 10'000)

Transfert technologique

Cahier des charges pour l'imagerie médicale

1. **Cristaux**
   - Densité élevée (> 7 g/cm^3)
   - Emissionrapide (< 100 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**
   - Sytèmes 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?

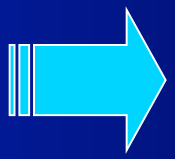
Limite liée à la résolution de l'instrument

Limite liée au bruit de fond

Cas réel: combinaison des 2 effets

L'imagerie médicale du futur

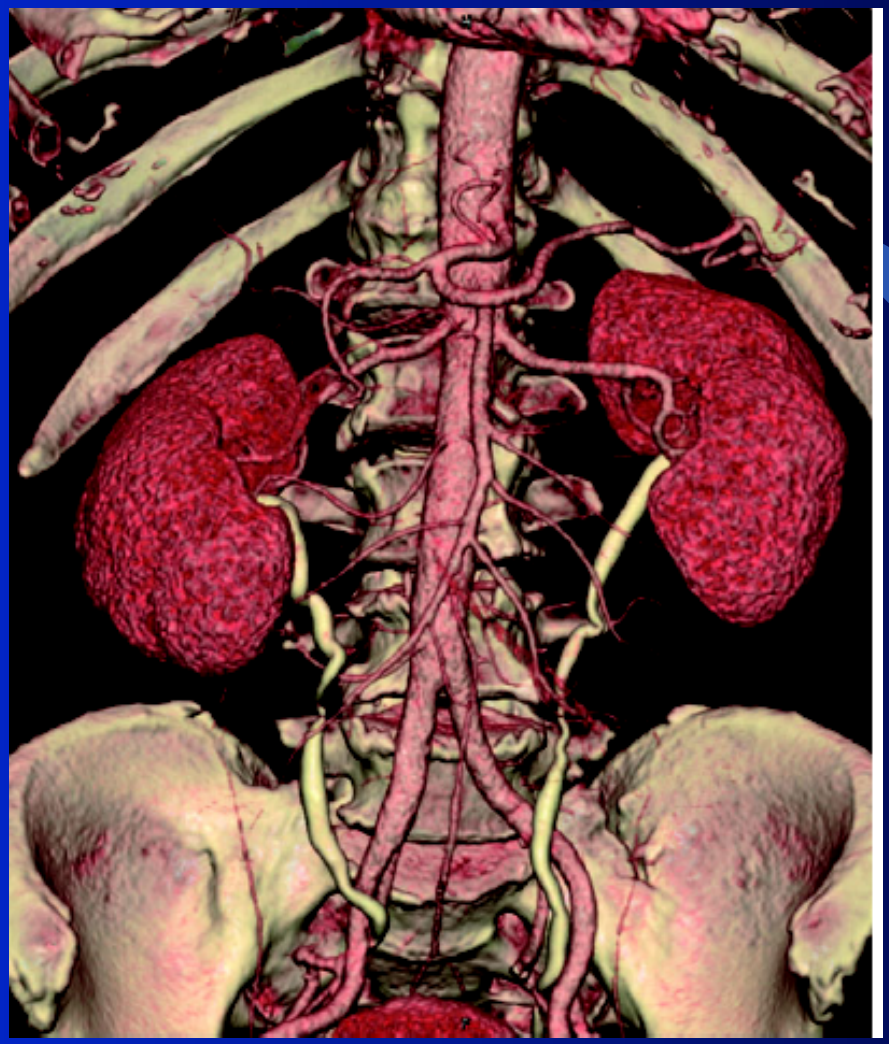
- Examens plus rapides
- Correction de mouvements
  - Respiration
  - Battements cardiaques
  - Bolus digestif
- Etudes dynamiques
- Quantification
- Multimodalité
- Réduire la dose aux patients



AMELIORER

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

La quête pour une meilleure résolution spatiale

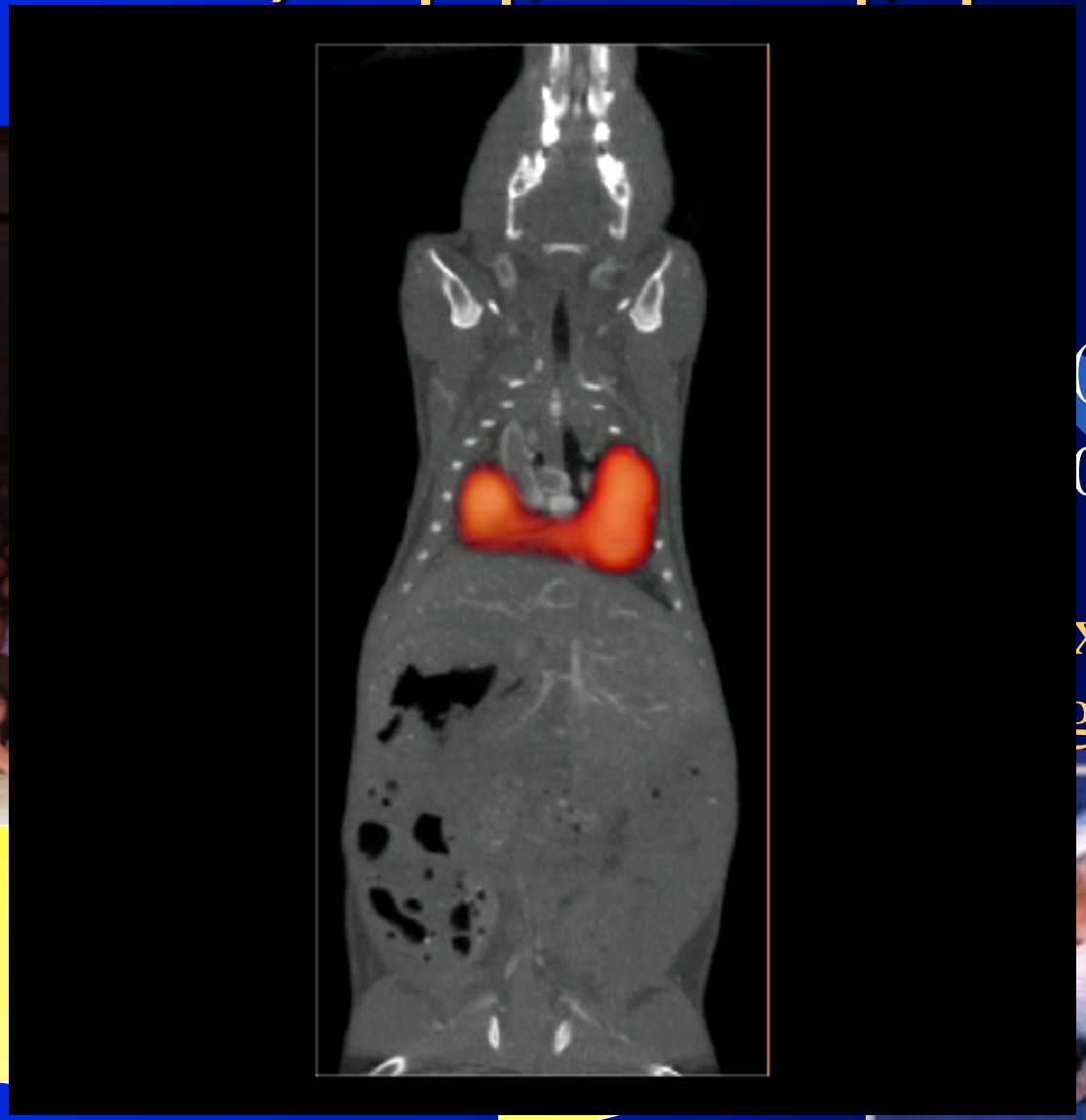


Siemens Somatom CT 64 slices

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



(x 300)

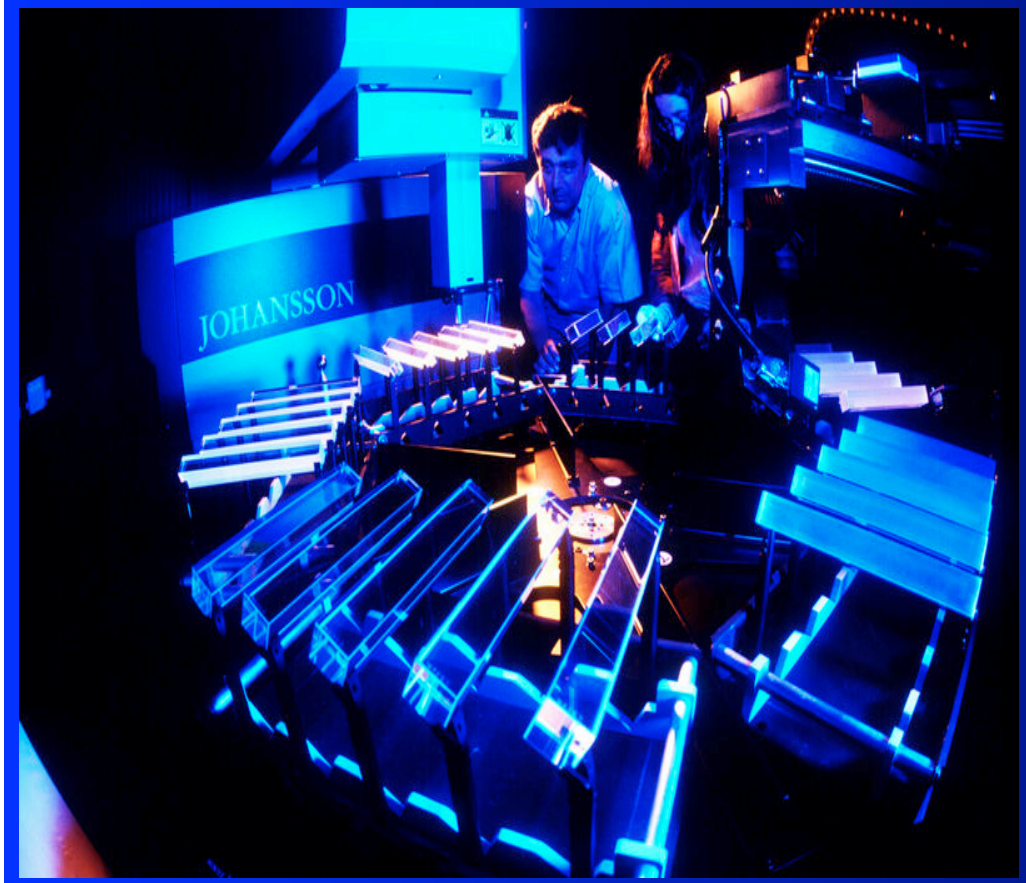
0)

x réclame des

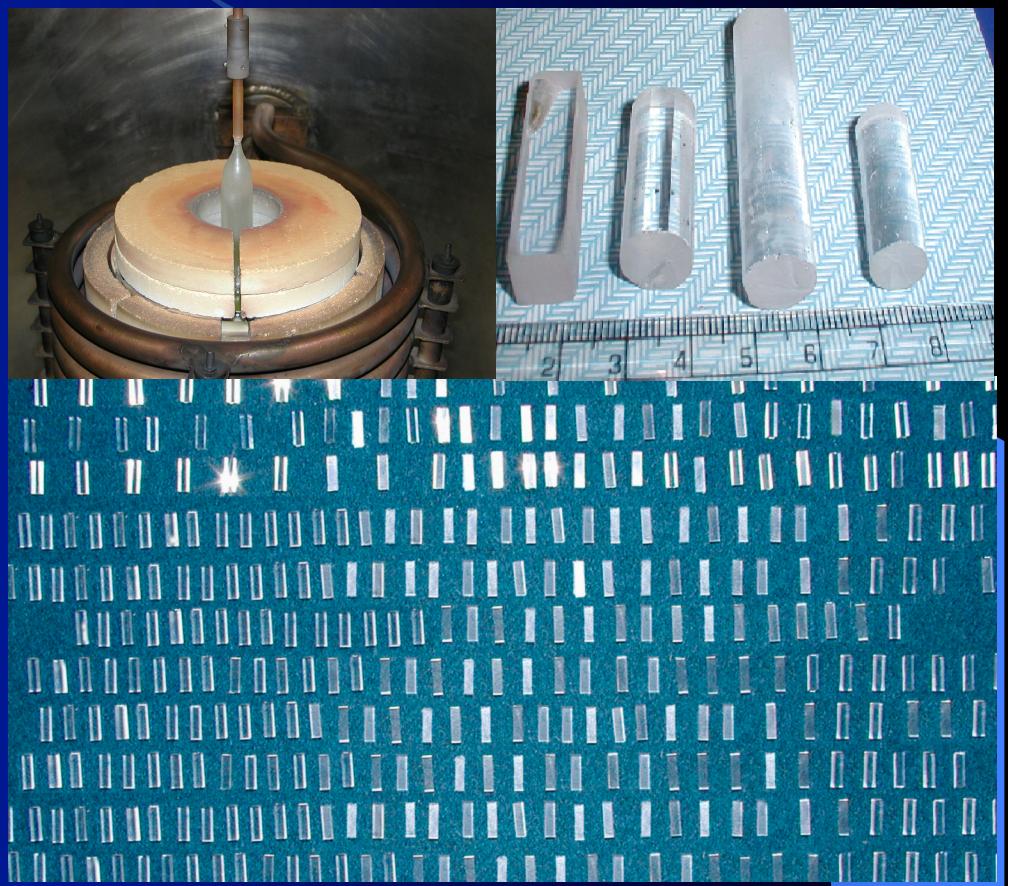
gration et à

1- Cristaux

CMS $PbWO_4$ production



Crystal Clear LuAP production



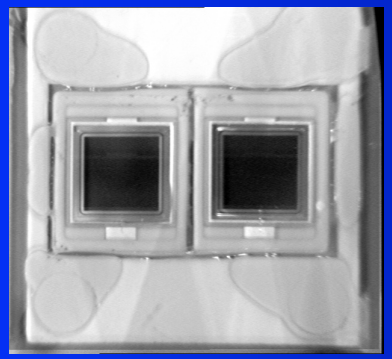
Scintillators for PET

Scintillators for PET

	1962	1977	1995	1999	2001	2003	2007
	NaI	BGO	GSO:Ce	LSO:Ce	LuAP:Ce	$LaBr_3$:Ce	LuAG:Ce
Density (g/cm^3)	3.67	7.13	6.71	7.40	8.34	5.29	6.73
Atomic number	51	75	59	66	65	47	63
Photofraction	0.17	0.35	0.25	0.32	0.30	0.13	0.30
Decay time (ns)	230	300	30-60	35-45	17	18	60
Light output (hν/MeV)	43000	8200	12500	27000	11400	70000	>25000
Peak emission (nm)	415	480	430	420	365	356	535
Refraction index	1.85	2.15	1.85	1.82	1.97	1.88	1.84

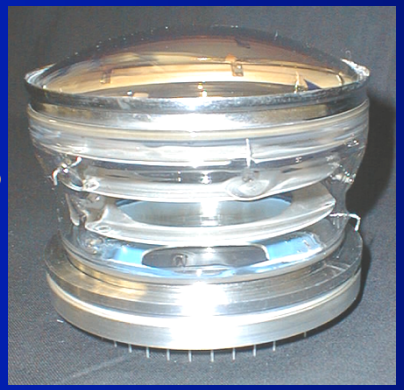
2- Photodetecteurs

CMS



Hamamatsu single channel APD

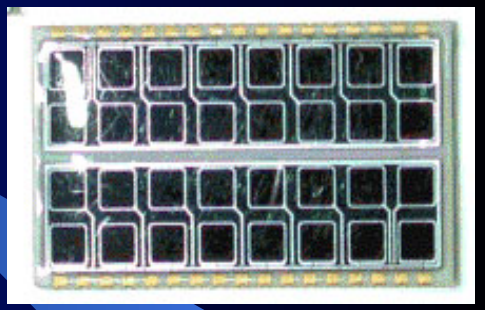
LHCB



BrainPET

HPD tube manufactured at CERN: 2048 channels

ClearPEM



Hamamatsu 32 channels APD array

Opera

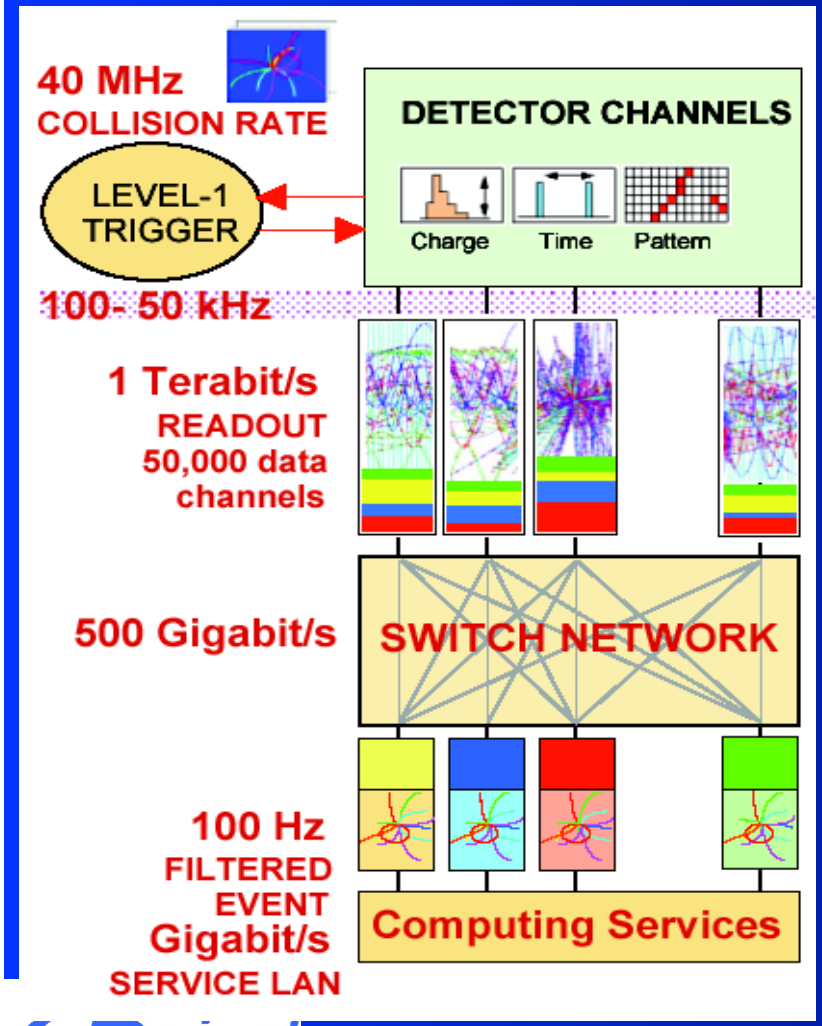
ClearPET

Mammography

Hammamatsu PM flat pannel

3- Architectures Pipeline

LHC

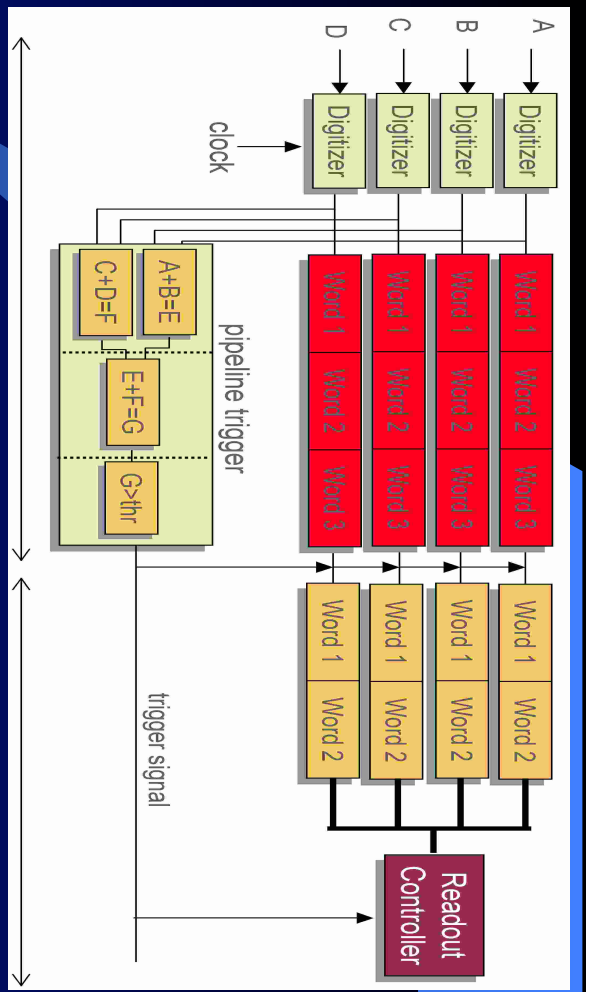


Digitisation

Pipeline

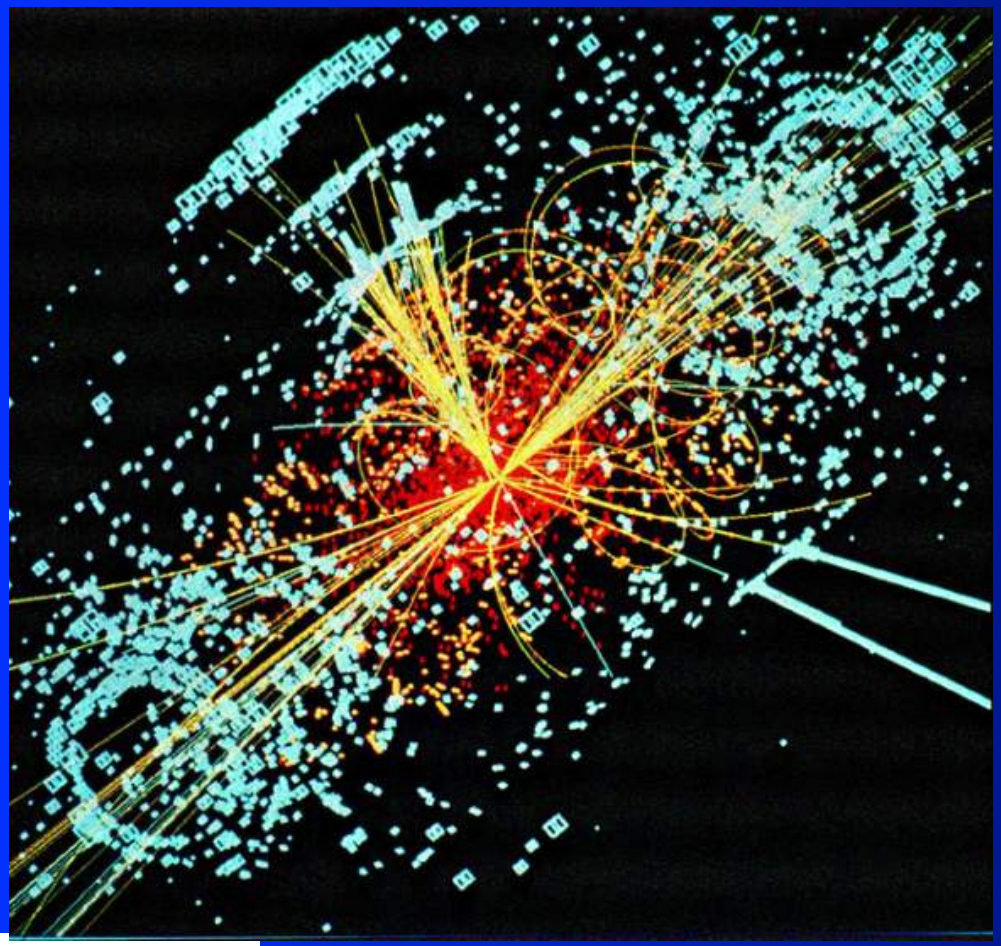
Event builder

Modern PET

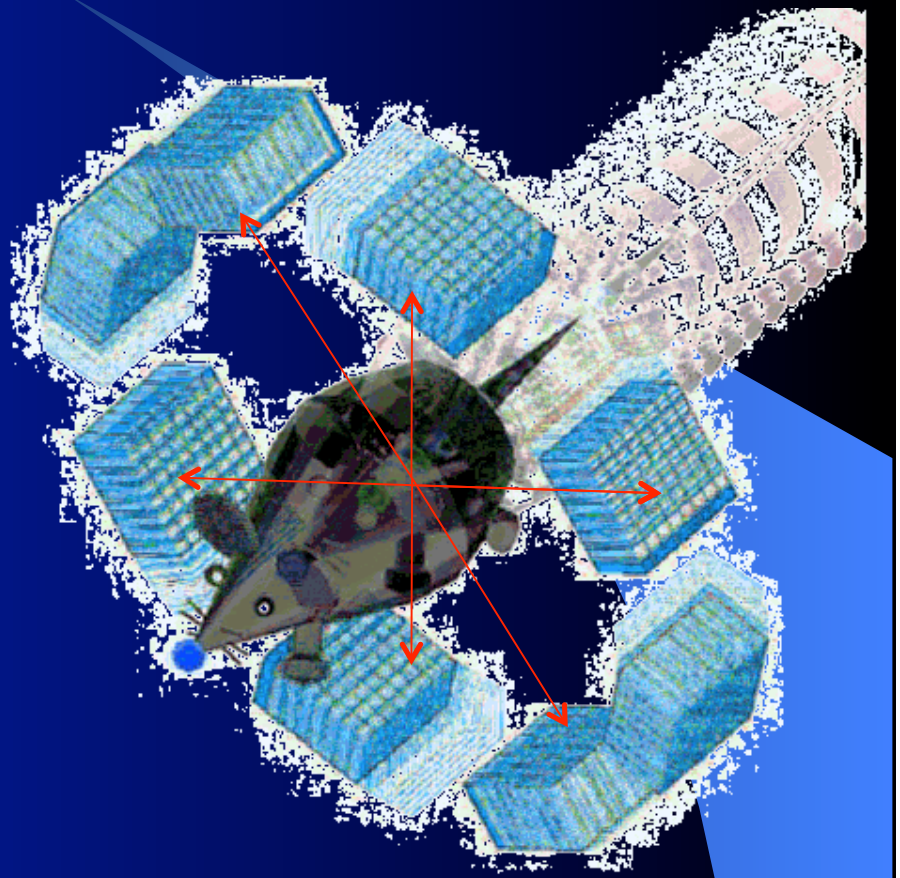


4- Simulation

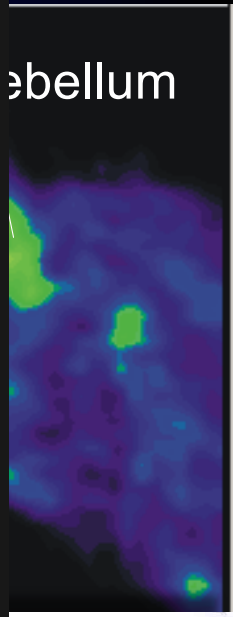
Higgs event at LHC (CMS) with Geant4

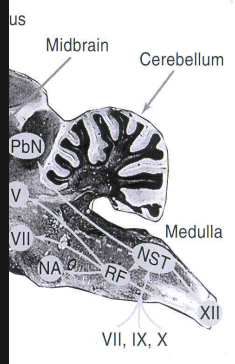


ClearPET with GATE: Geant4 Application for Tomographic Emission



ClearPET®, TEP petit animal





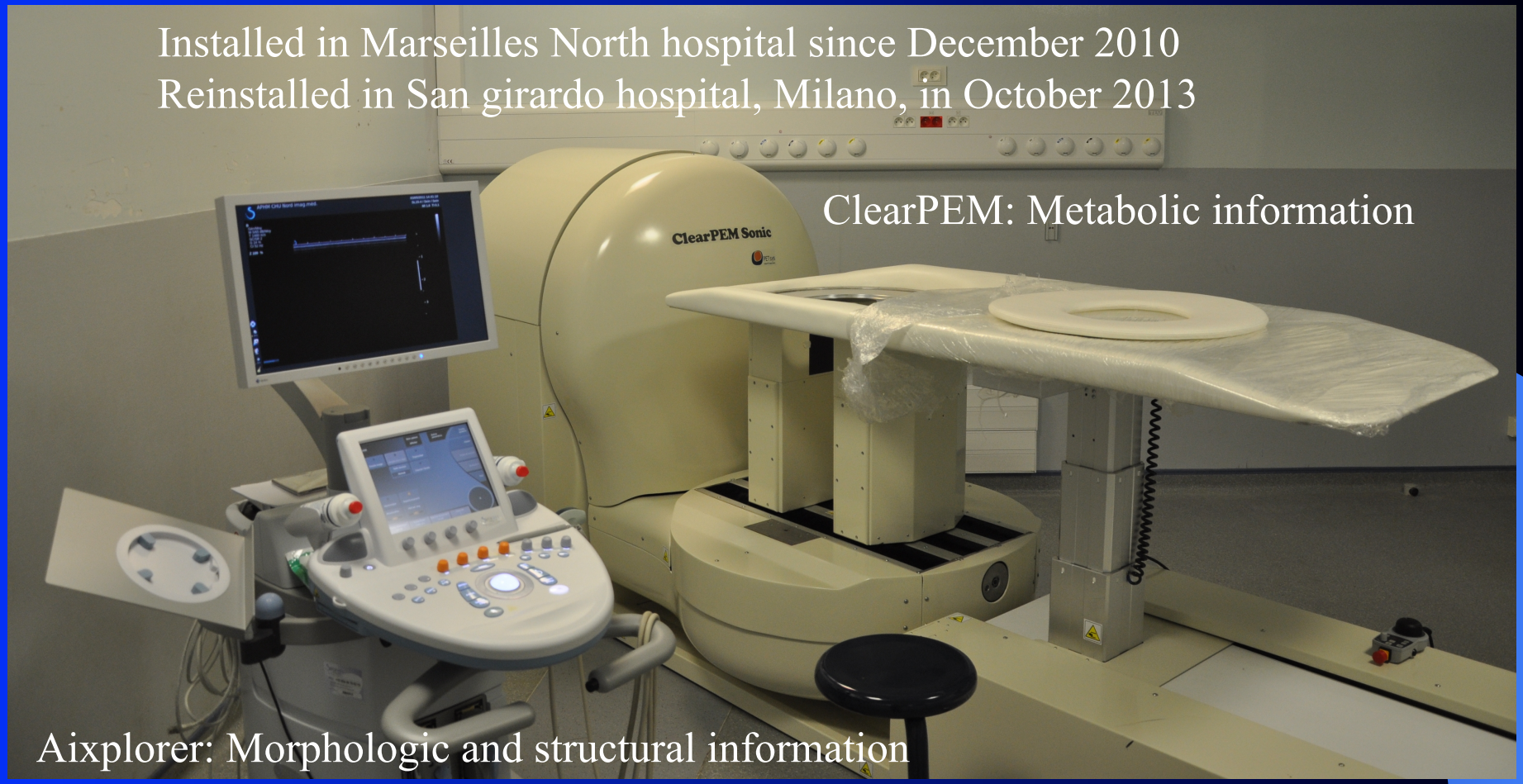
Etudes de plus en plus spécifiques sur modèles animaux

- L'imagerie petit animal se fait généralement sous anesthésie
- L' anesthesie modifie les fonctions cervicales et biaise les études neuro-physiologiques
- RATCAP, developé à BNL est un TEP miniaturisé et portable pour animal éveillé
- 12 blocs de 4x8 cristaux de LSO 2x2x5mm^3 lus par des matrices de 4x8 APD et 0.18µm CMOS ASIC

•C. Woody et al. Several papers in conference records of NSS/MIC2004, Rome

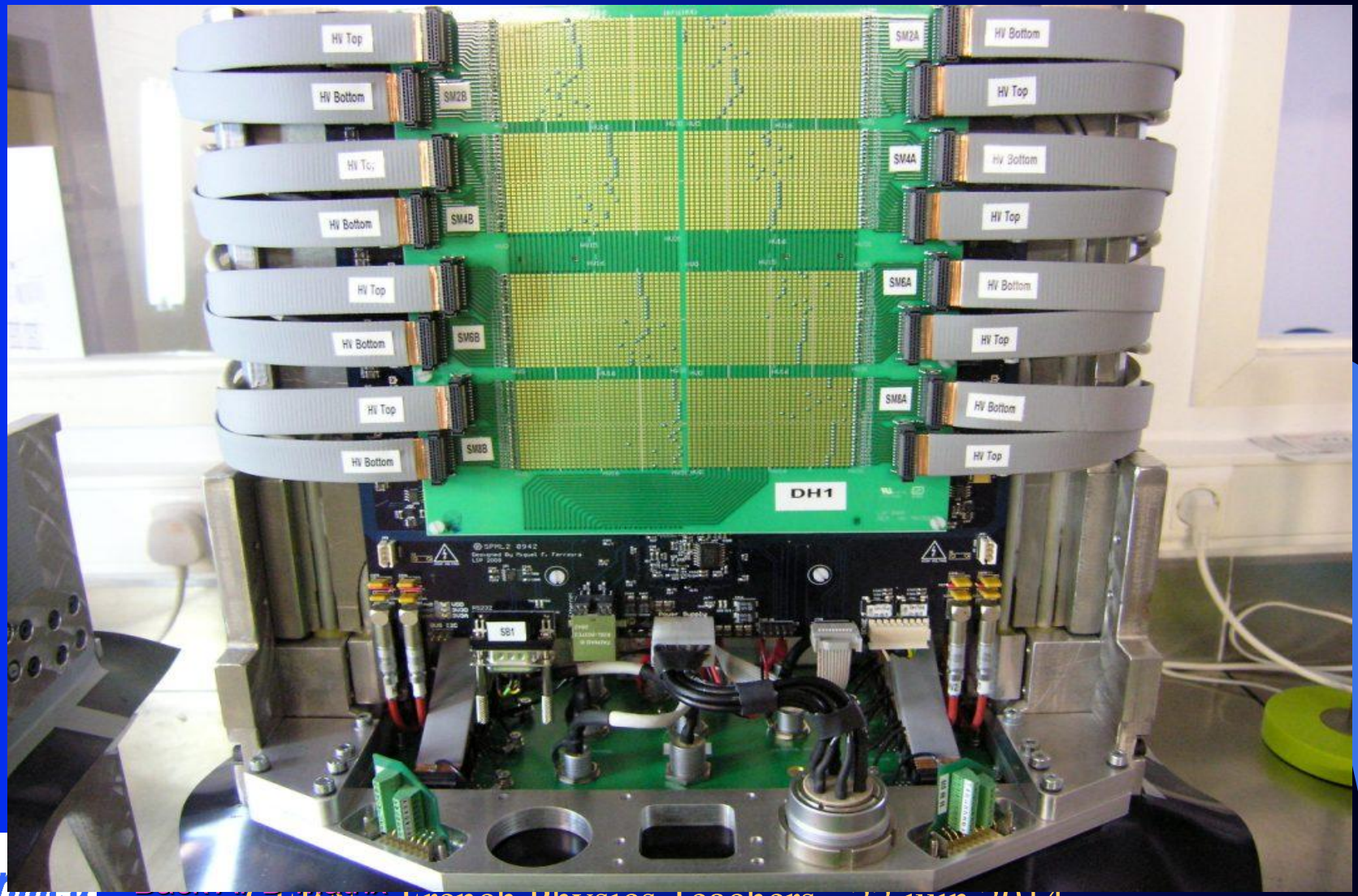
Courtesy of C. Woody,BNL

ClearPEM-Sonic a collaborative project between physicians and physicists



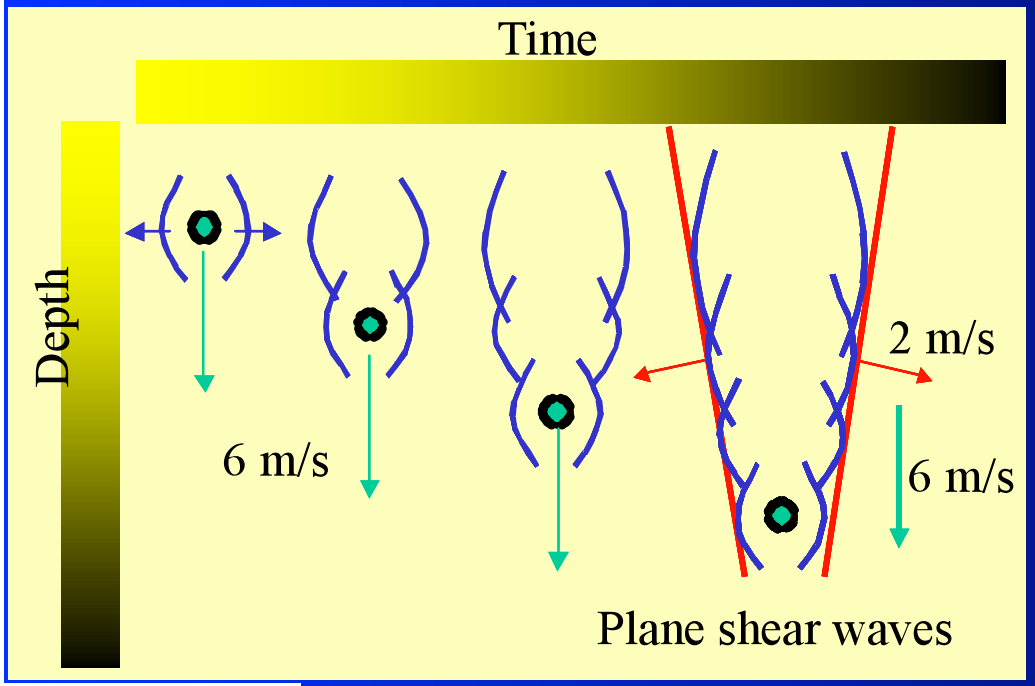
Objective: Detect 3mm tumors and define their cancerous status

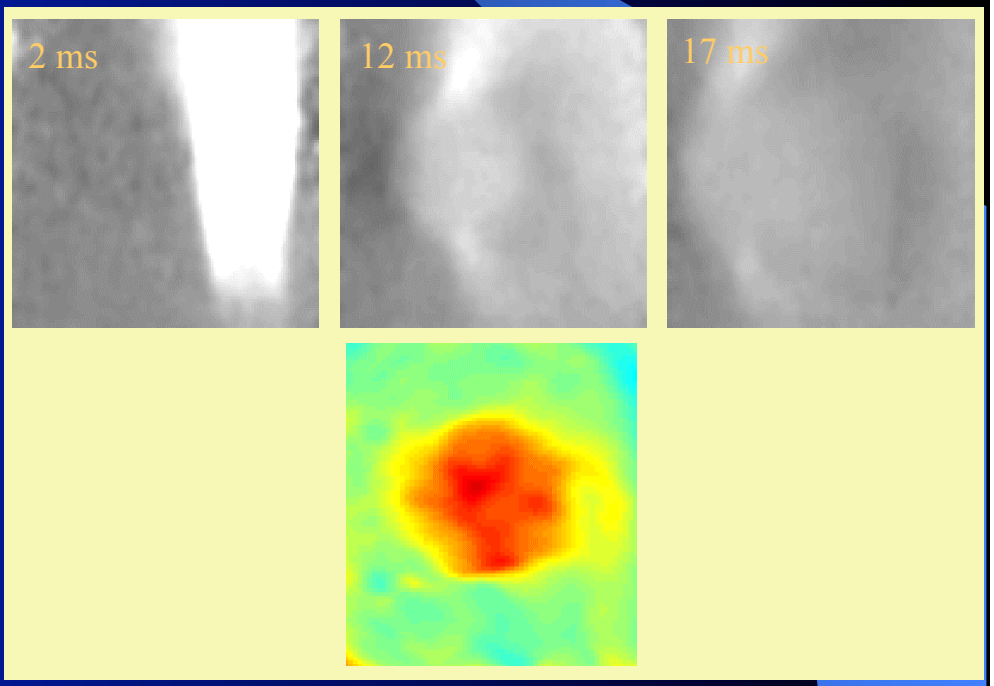
Des technologies d'avant-garde ClearPEM



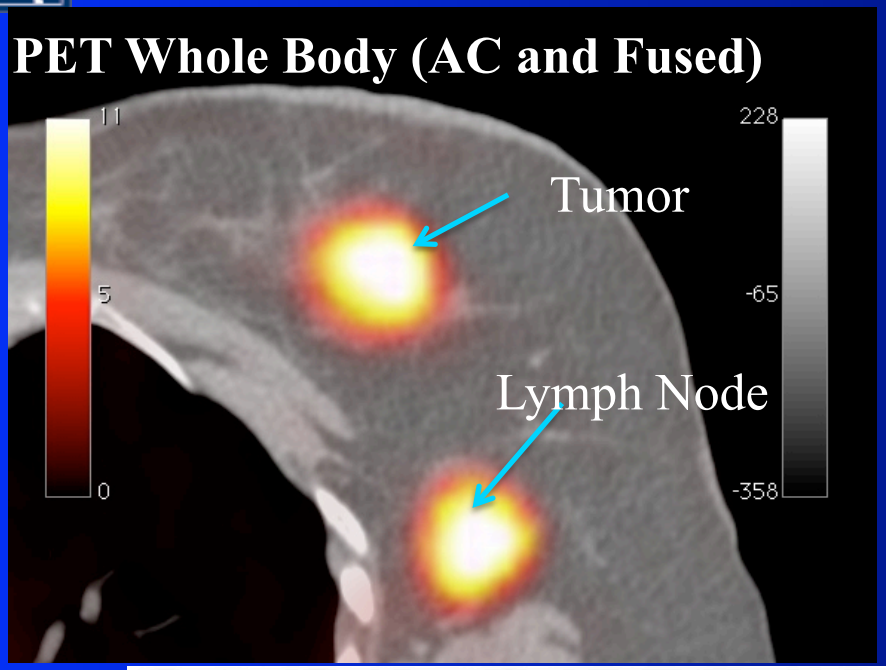
New technologies
Ultrasound

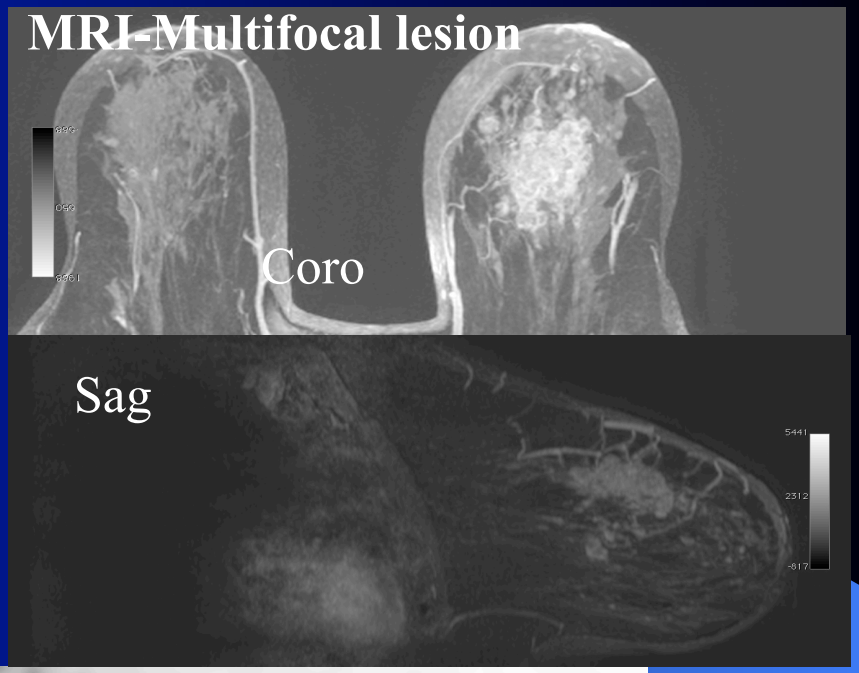
- Focus ultrasound beam in tissue
- Propagate focal point a t supersonic speed in breast
- Measure the deformation of the shock wave by a tumor

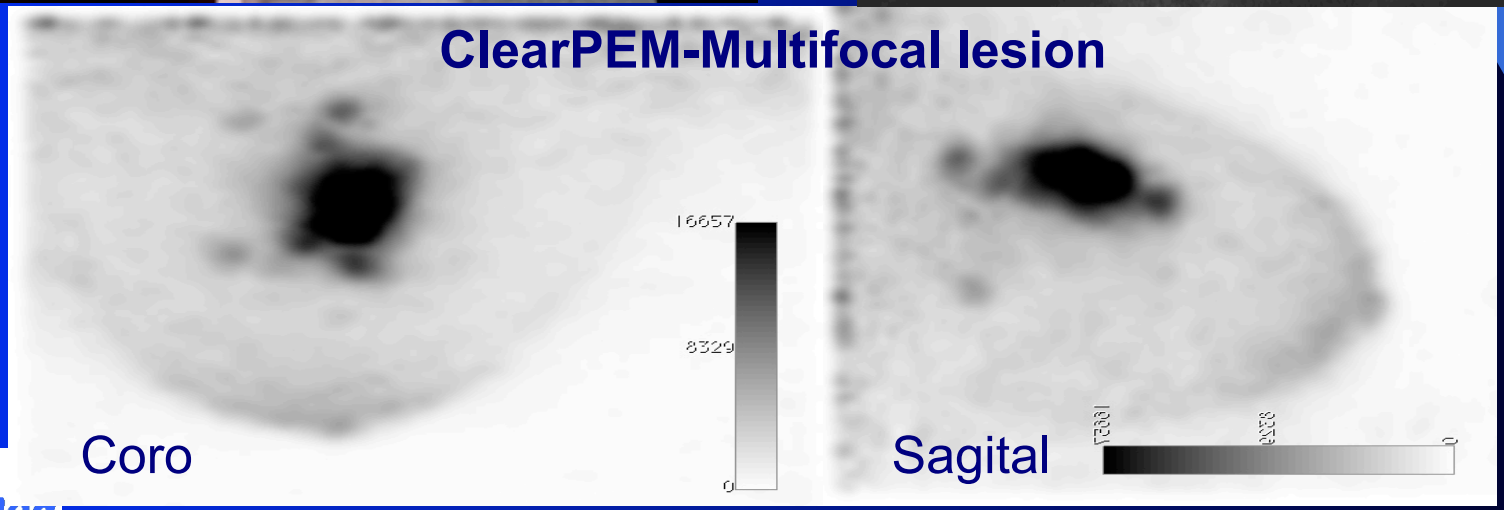




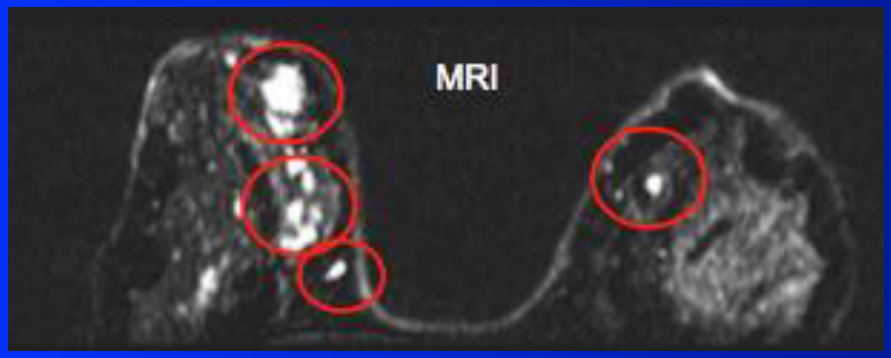
Benefit of dedicated breast PET imaging







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

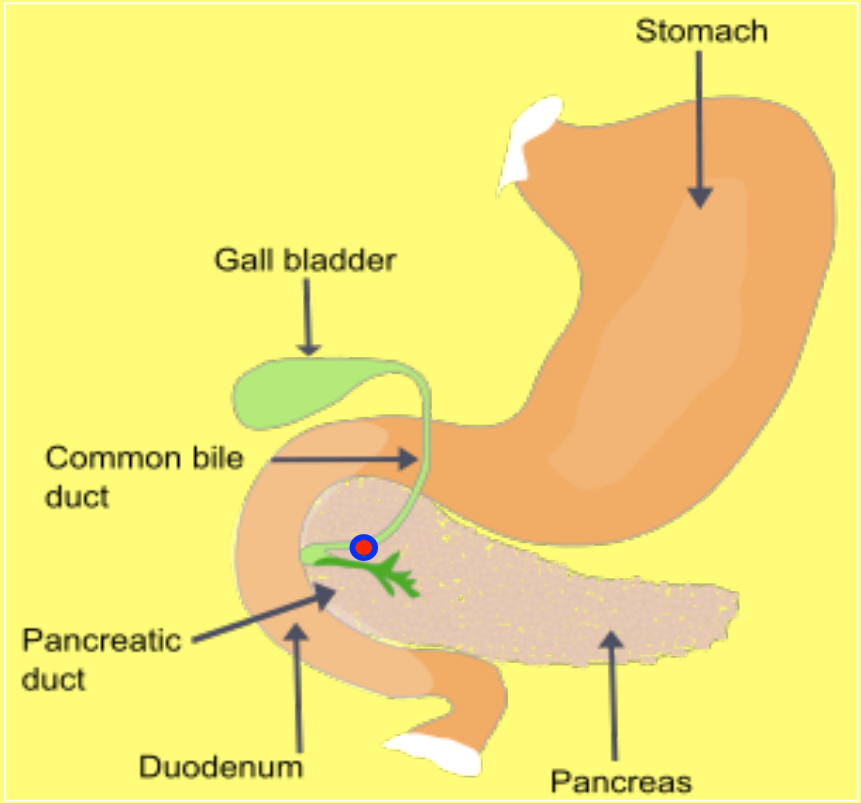
P. Lecoq
CERN, Geneva, Switzerland

Imaging tool for pancreas and prostate cancer biomarker development

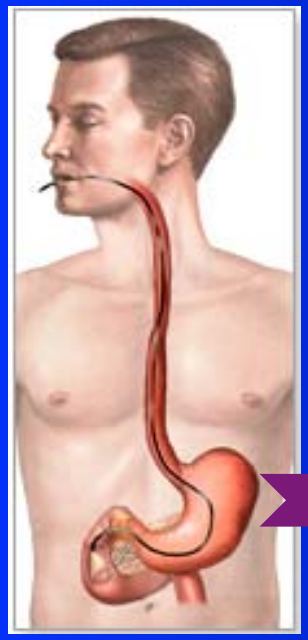
Objectives

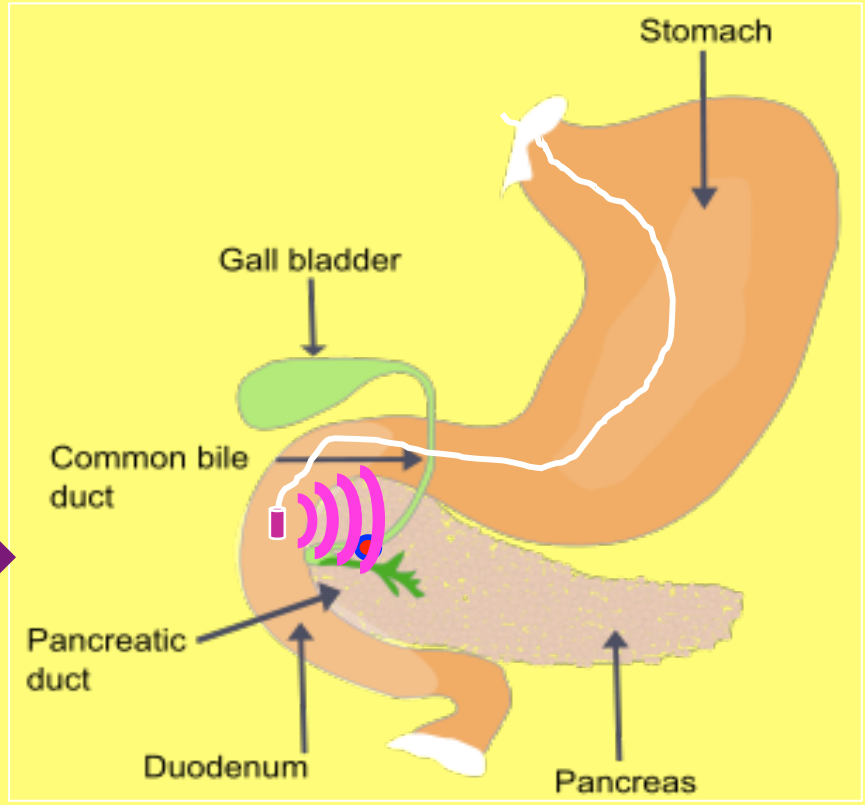
- Develop new biomarkers for pancreas and prostate cancer
  - Ex: mAb16D10 antibody for pancreas
  - Ex: ^{68}Ga – PSMA for prostate
- Introduce PET as an endoscopic imaging tool
- Develop intra-operative interventional imaging techniques

EndoTOFPET-US: The Principle

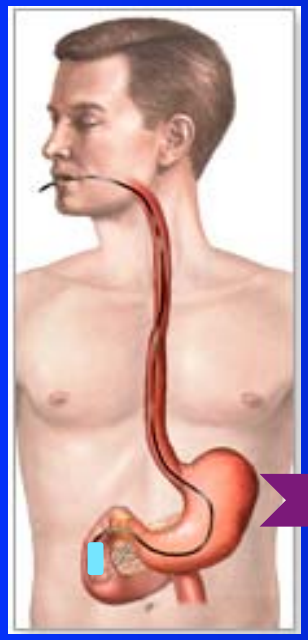


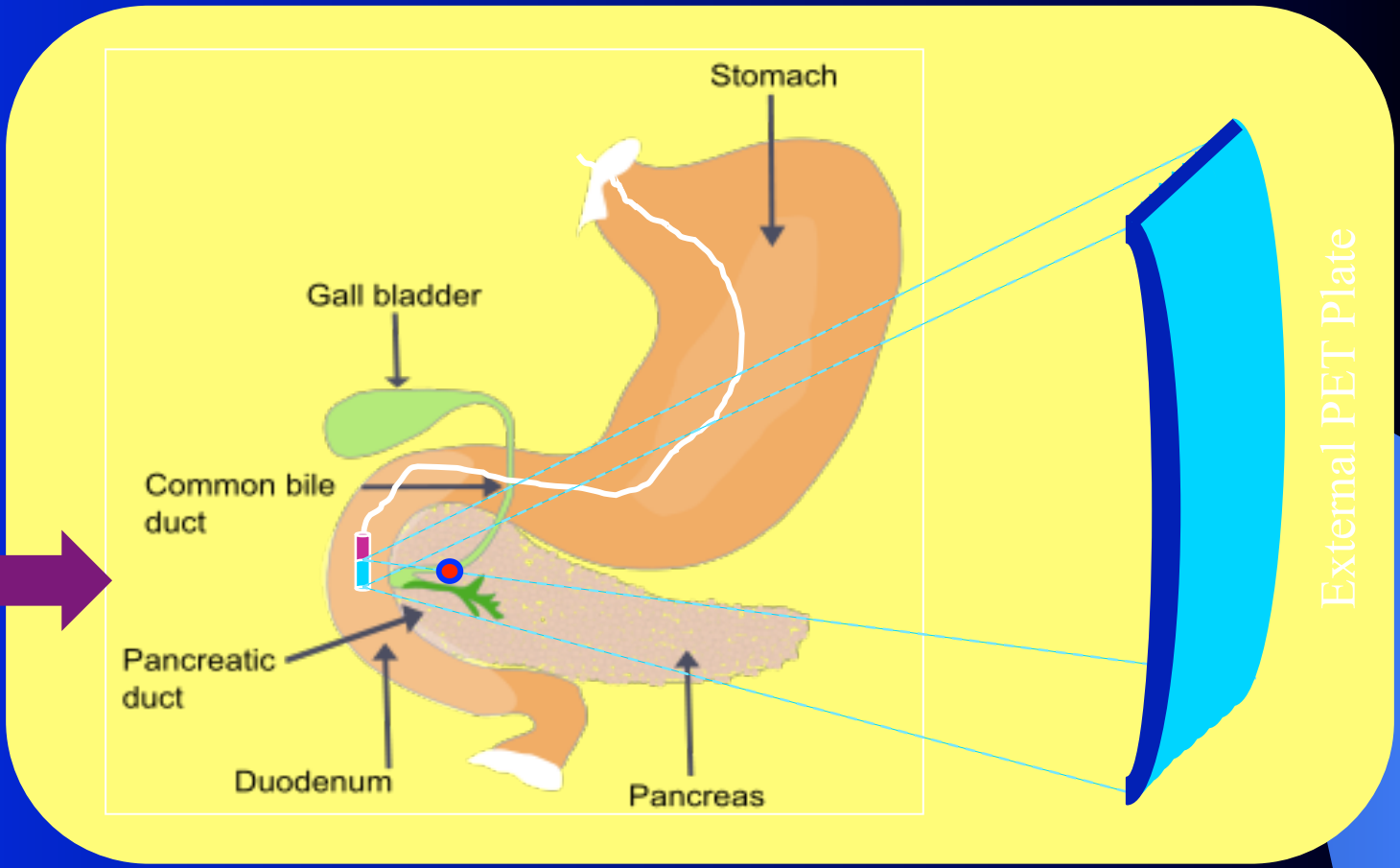
EndoTOFPET-US: The Principle





EndoTOFPET-US: The Principle





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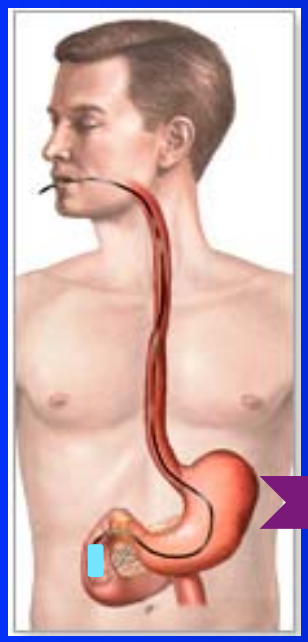

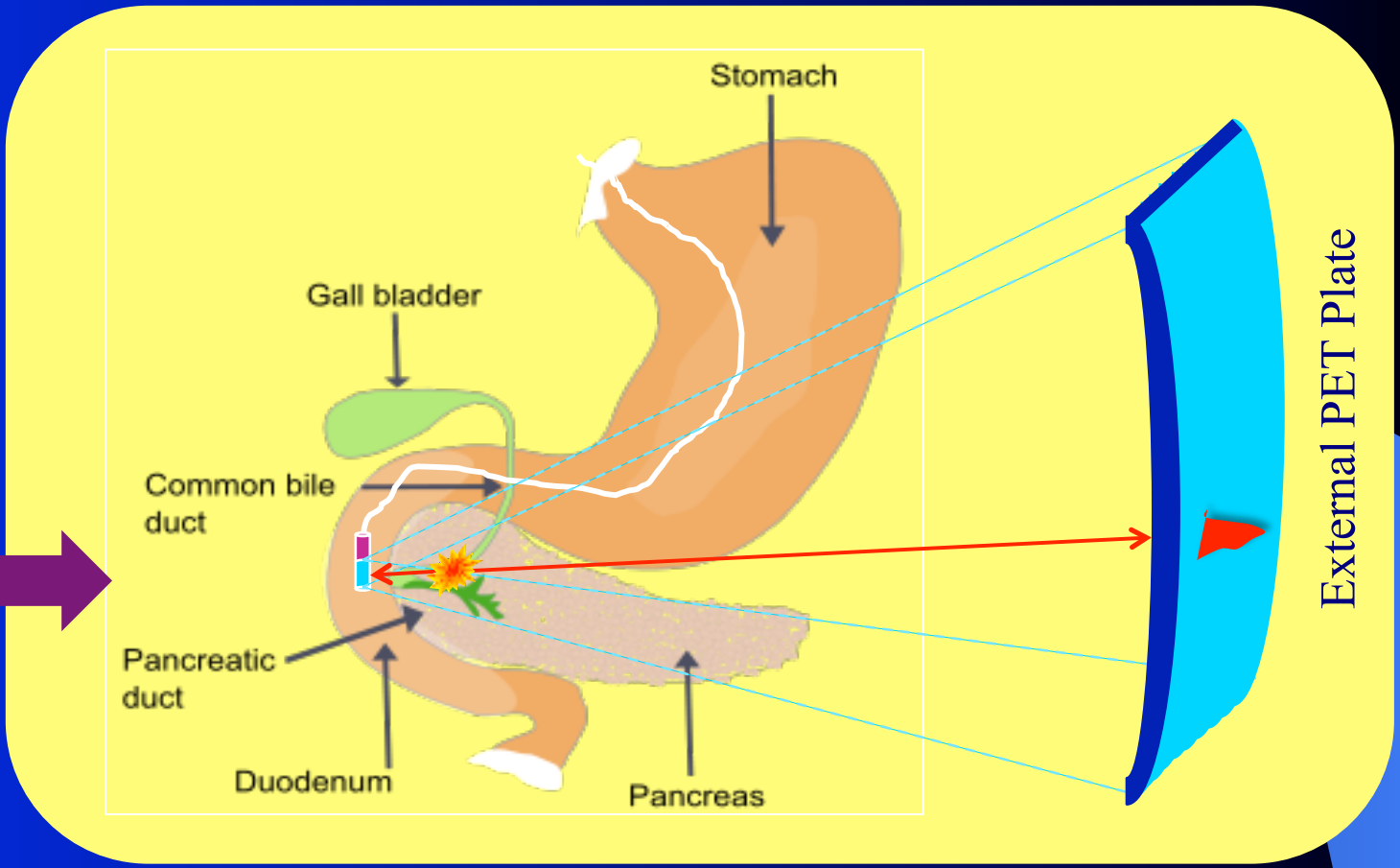

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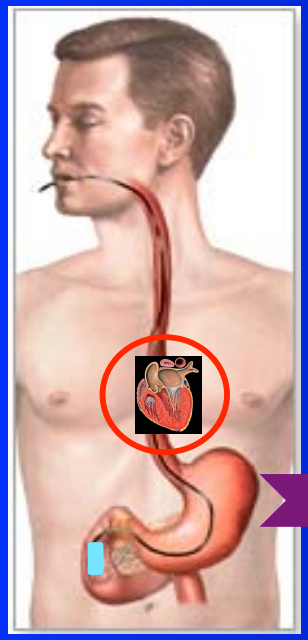
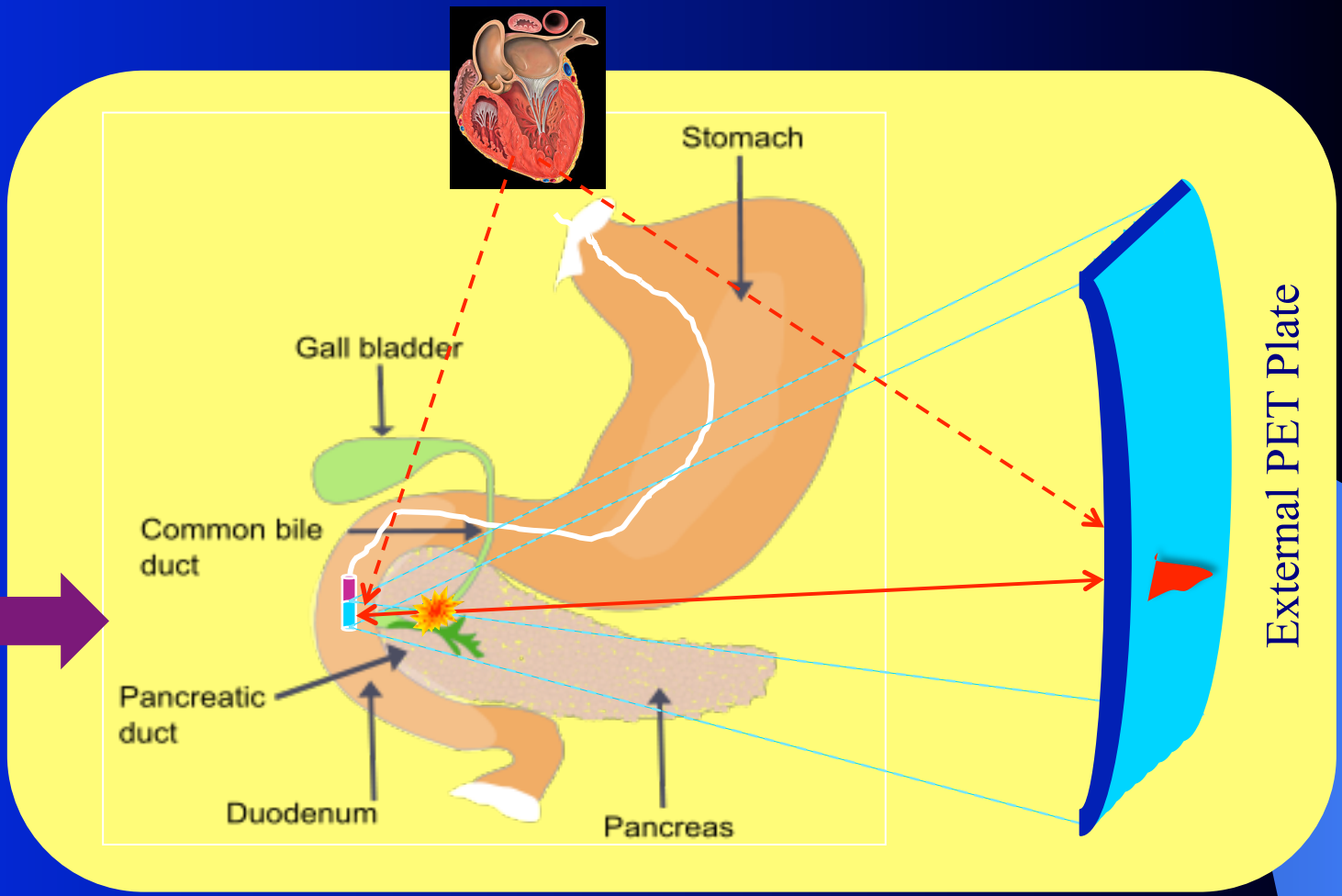
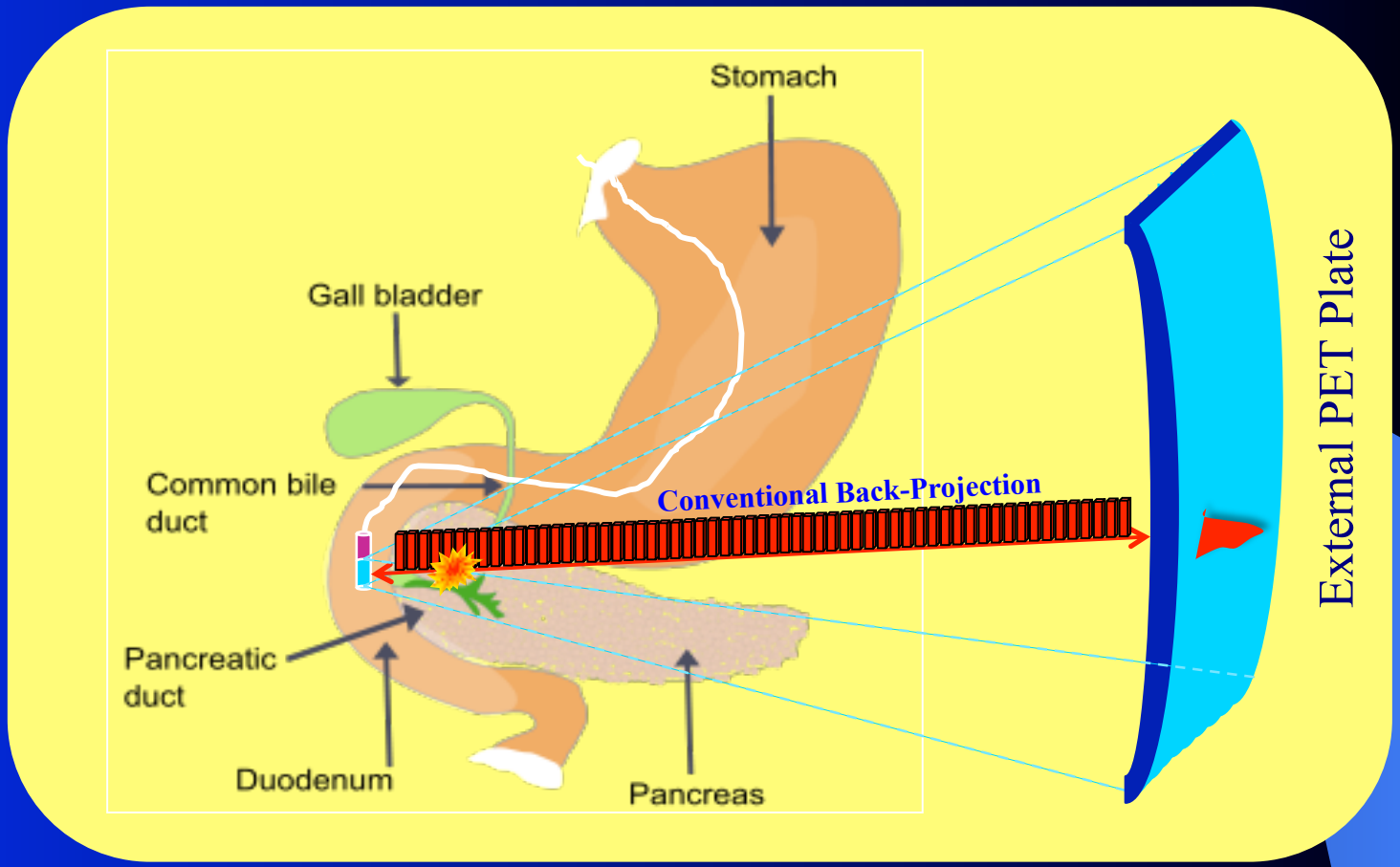
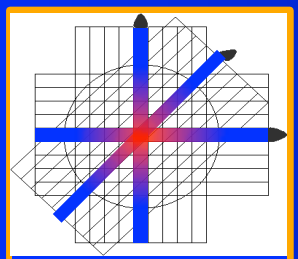




EndoTOFPET-US: The Principle

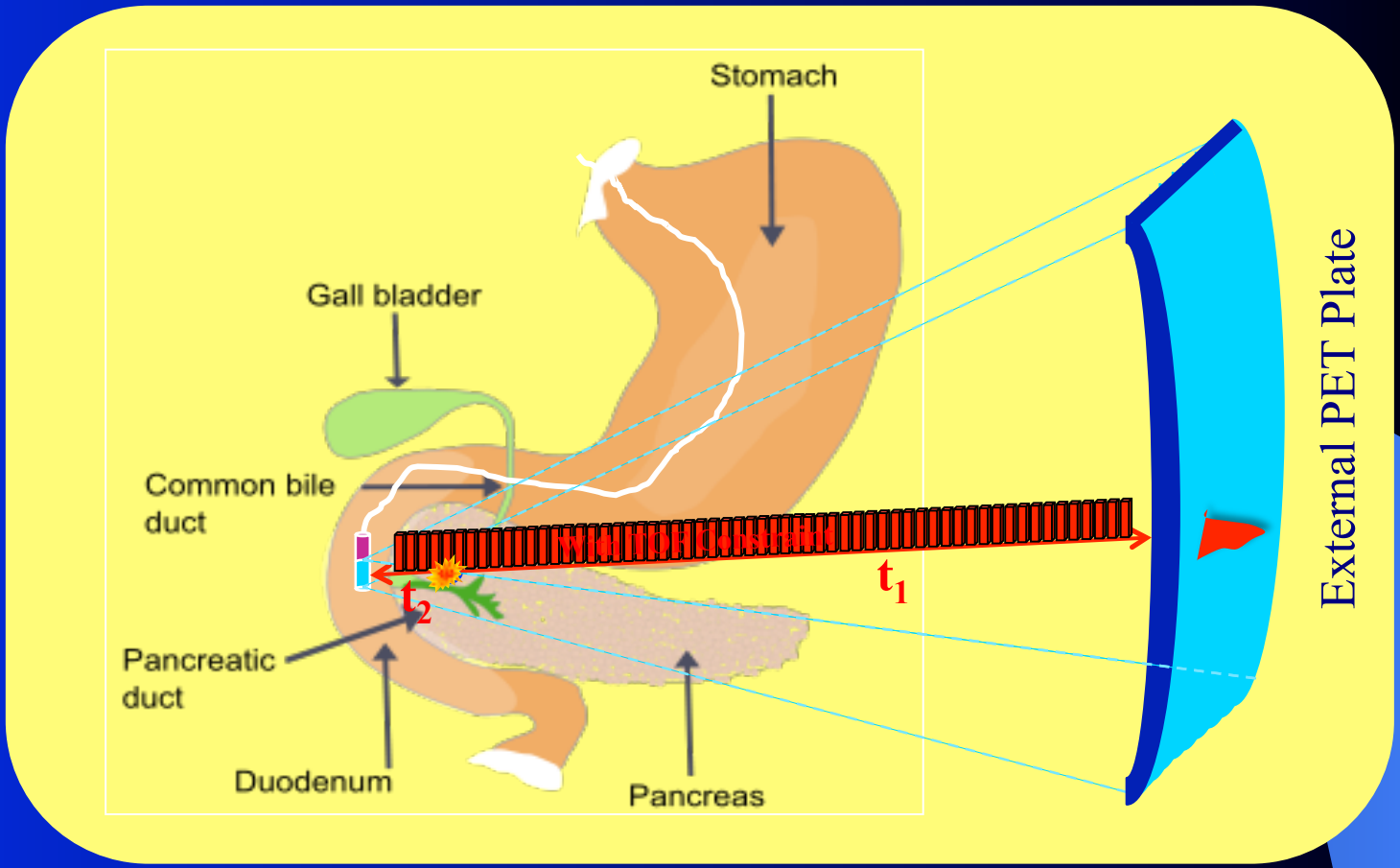


EndoTOFPET-US: Why TOF?



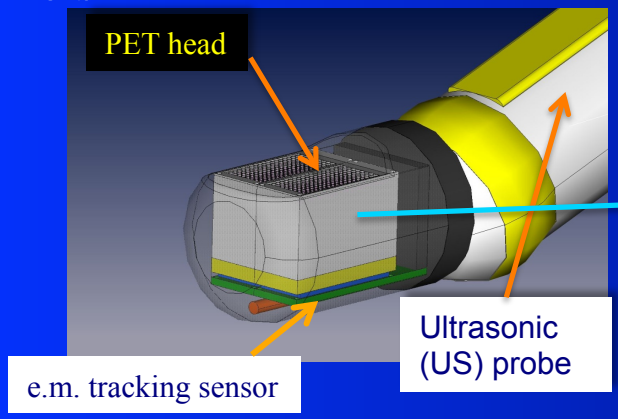
$$\Delta z = \left| \frac{t_2 - t_1}{2} \right| \times c$$

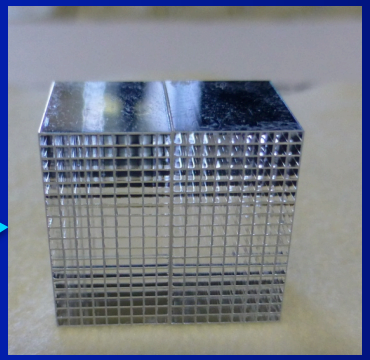
Target CTR: 200ps
→ 30mm *FWHM*



Technical design

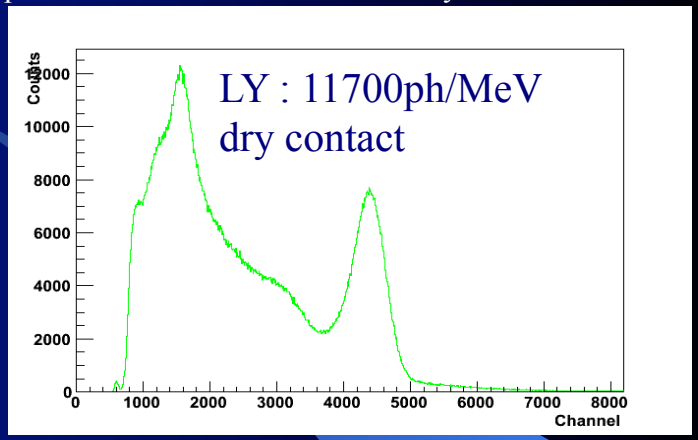
Internal probe : 1 or 2 matrices of 9x18 LYSO pixels



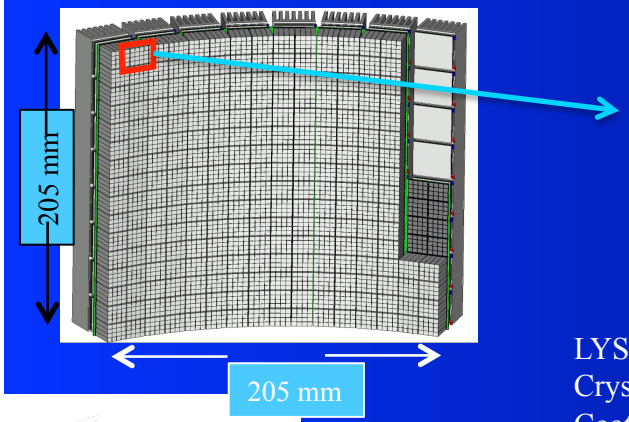


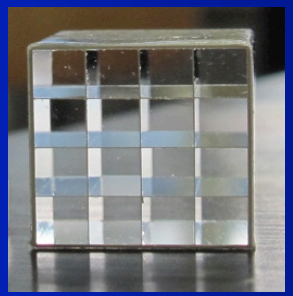
2 LYSO matrices from Proteus.
Crystal pitch: 800µm, length: 10mm
Coating: ESR reflector by 3M

Photopeak for entire matrix 9*18 with dry contact



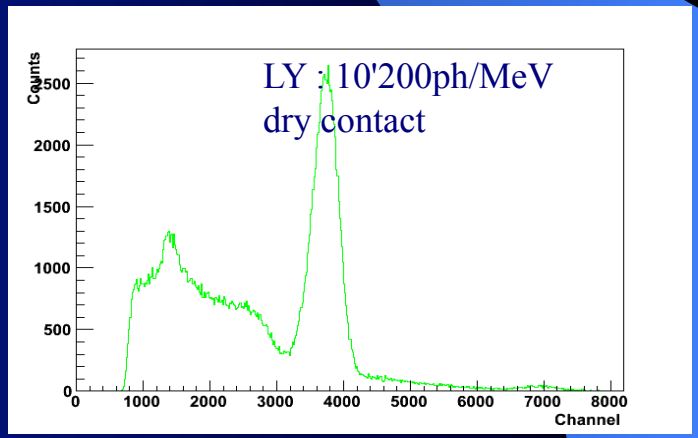
External plate: 256 matrices of 4x4 LYSO pixels





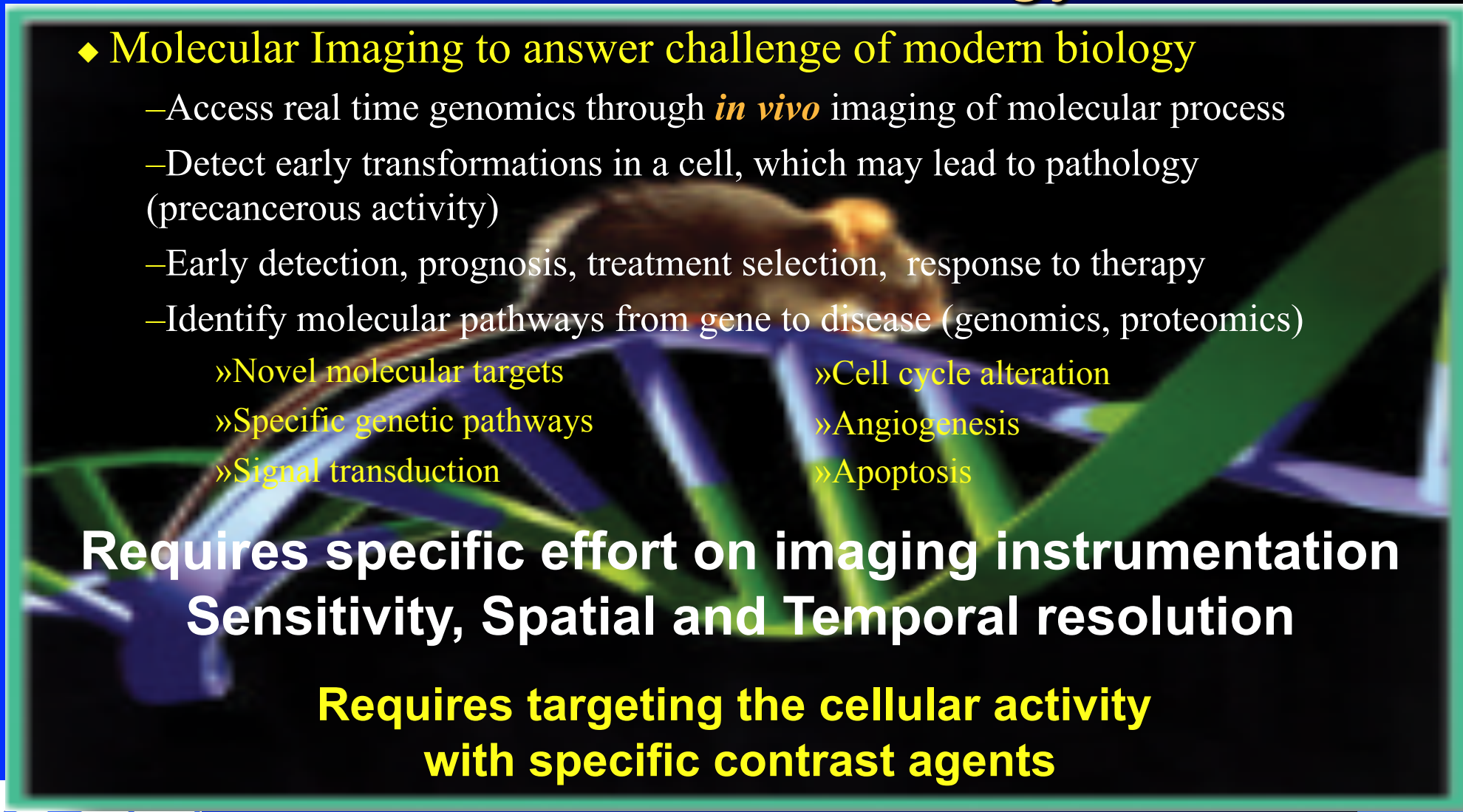
LYSO matrix from CPI
Crystal pitch: 3.2mm, length: 15mm
Coating: ESR reflector by 3M

Photopeak for entire matrix 4*4 with dry contact



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

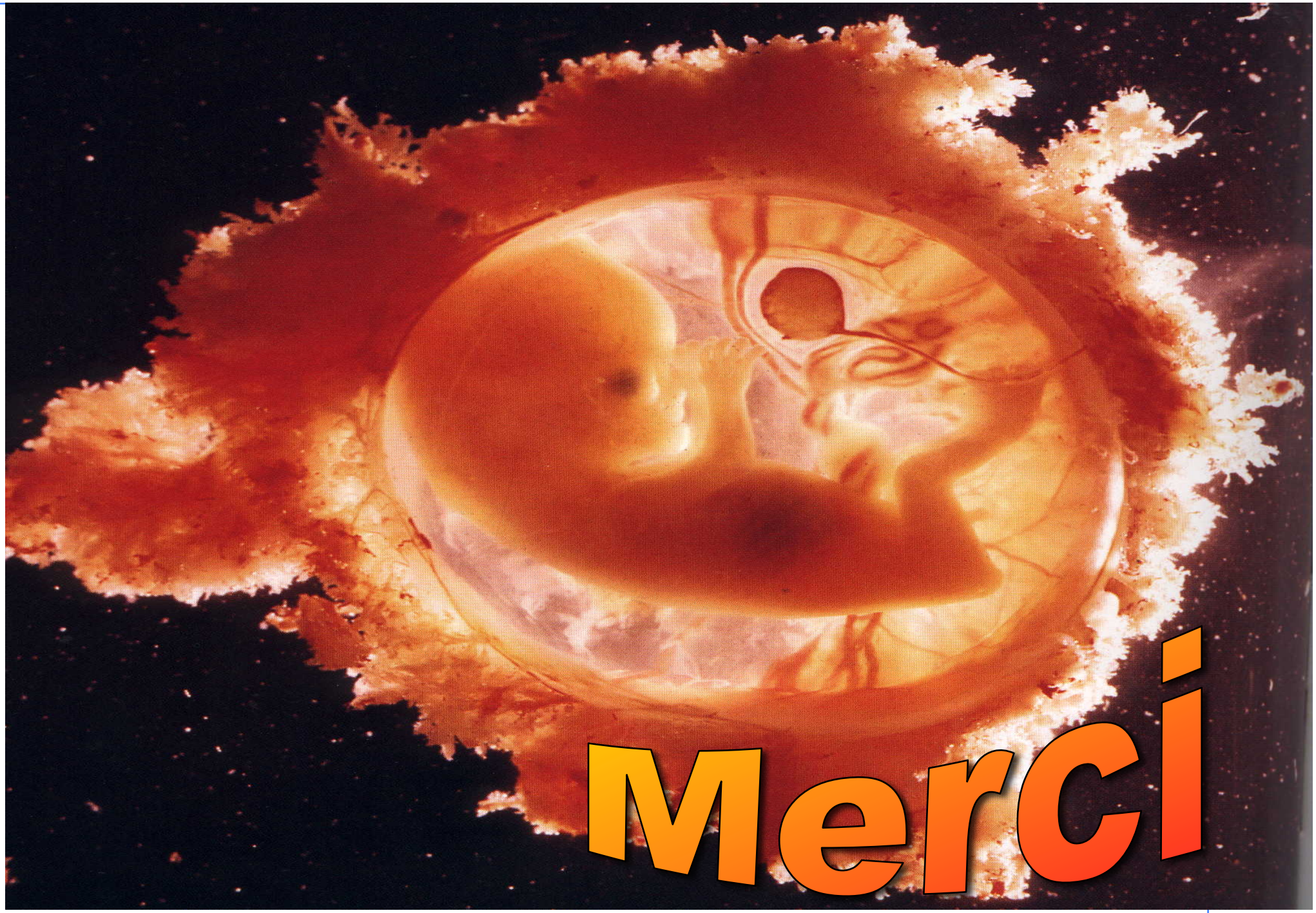
Molecular Imaging in Medicine & Biology



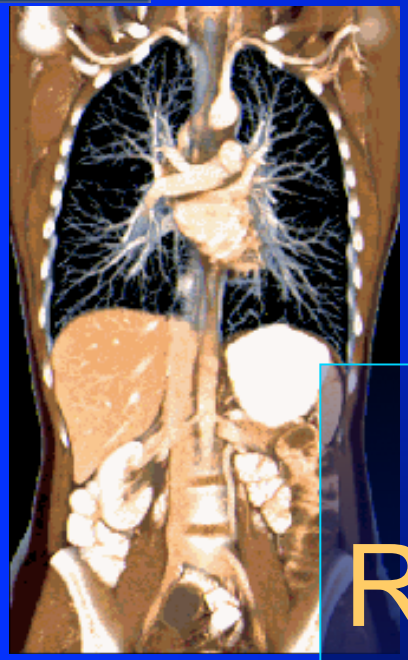
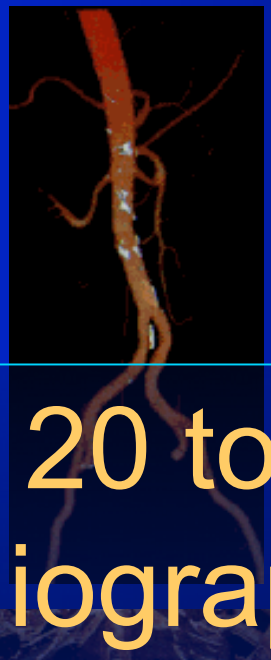
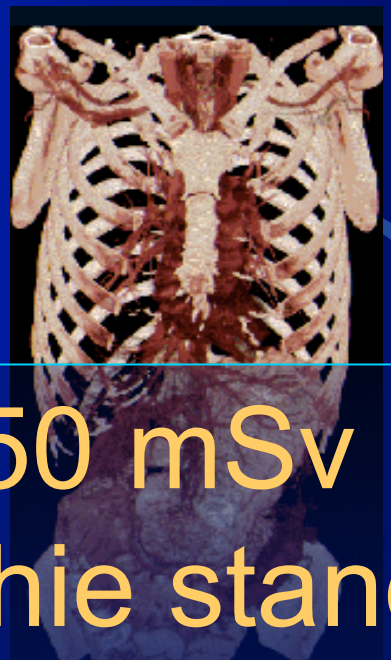
- Molecular Imaging to answer challenge of modern biology
  - –Access real time genomics through ***in vivo*** imaging of molecular process
  - –Detect early transformations in a cell, which may lead to pathology (precancerous activity)
  - –Early detection, prognosis, treatment selection, response to 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

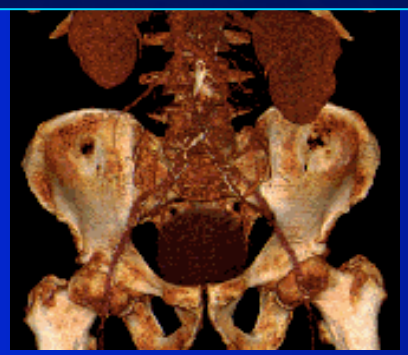

MerCi

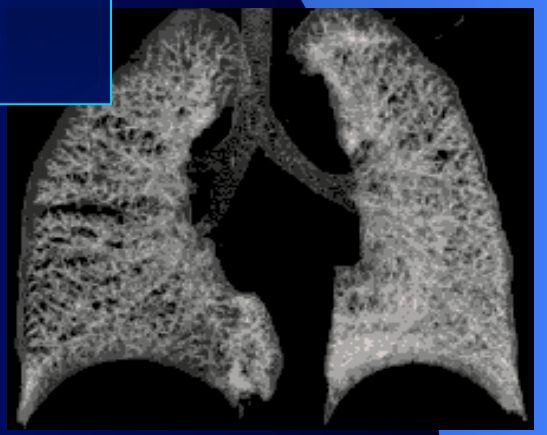
Exposition pour un scanner CT

< 0,4 sec/ rotation
Organ in a sec (17 cm/sec)
Whole body < 10 sec

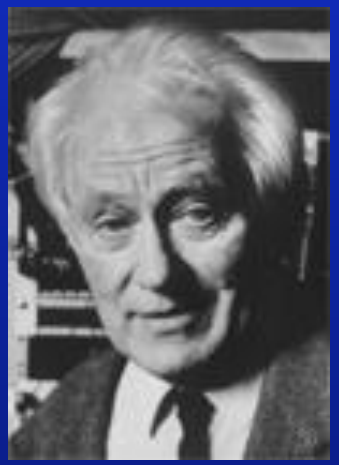
20 to 50 mSv
Radiographie standart
0.1 mSv



La chambre proportionnelle
Radiographie digitale à faible dose

Prix Nobel de Physique 1992



Georges Charpak
Physicien CERN

Photon counting in CT

Advantages of photon counting CT:

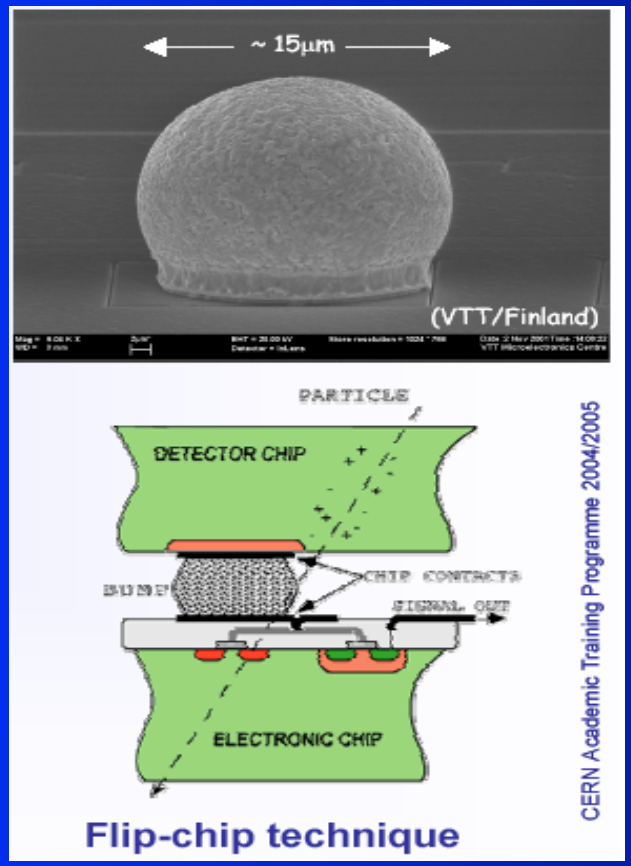
- Each event has equal weight independent of energy
  - ⇒ ***Elimination of weight factor proportional to energy of integration imaging***
  - ⇒ ***Closer to optimal weighting of E^{-3} ****
- Threshold detection allows discrimination of noise and scatter

Requirements :

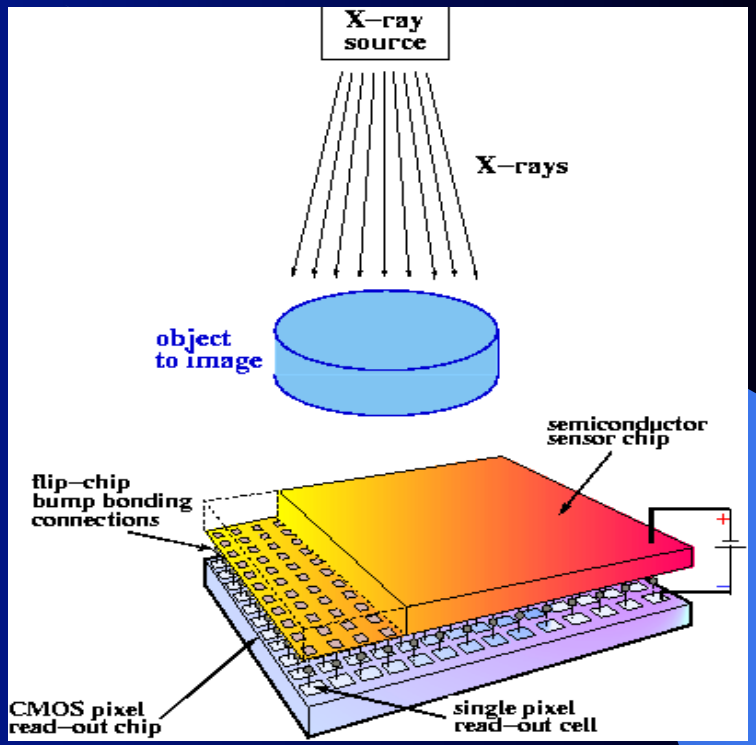
- Detector: high sensitivity to low-energy X-rays,
  high count rate capability
  ⇒ count-rate > 10^6 - 10^7 counts/s/pixel, *the higher the better*

* R.N. Cahn et al., "Detective quantum efficiency dependence on X-ray energy weighting in mammography", *Med. Phys.* 26 (12), pp. 2680-2683,

Détecteur hybride à pixels pour comptage de photons X

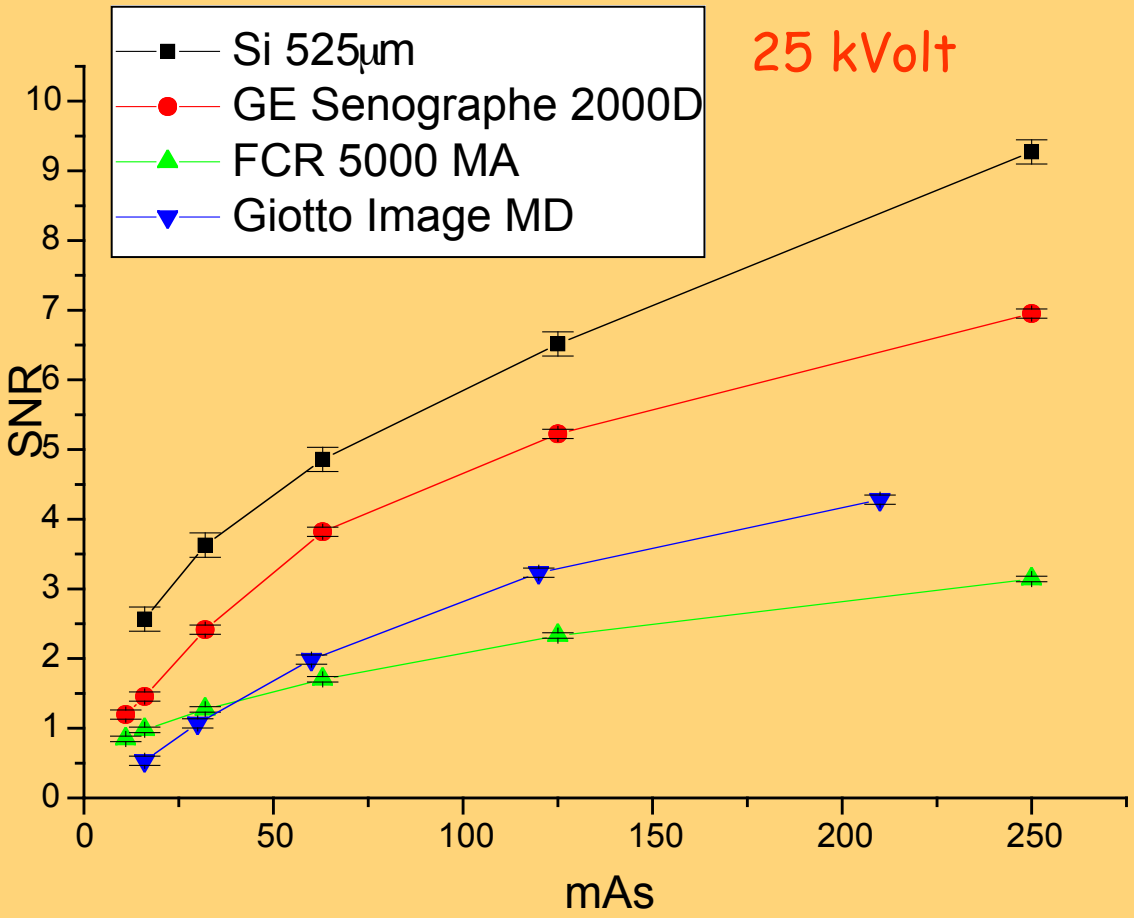


Détecteur pour les trajectographes du LHC



Détecteur Médipix pour les rayons X

Single photon counting versus integrating digital radiography



- SNR for 2 mm thick tumor mass (RMI 156 phantom)

M. G. Bisogni et al., NIMA 546, 14 (2005)