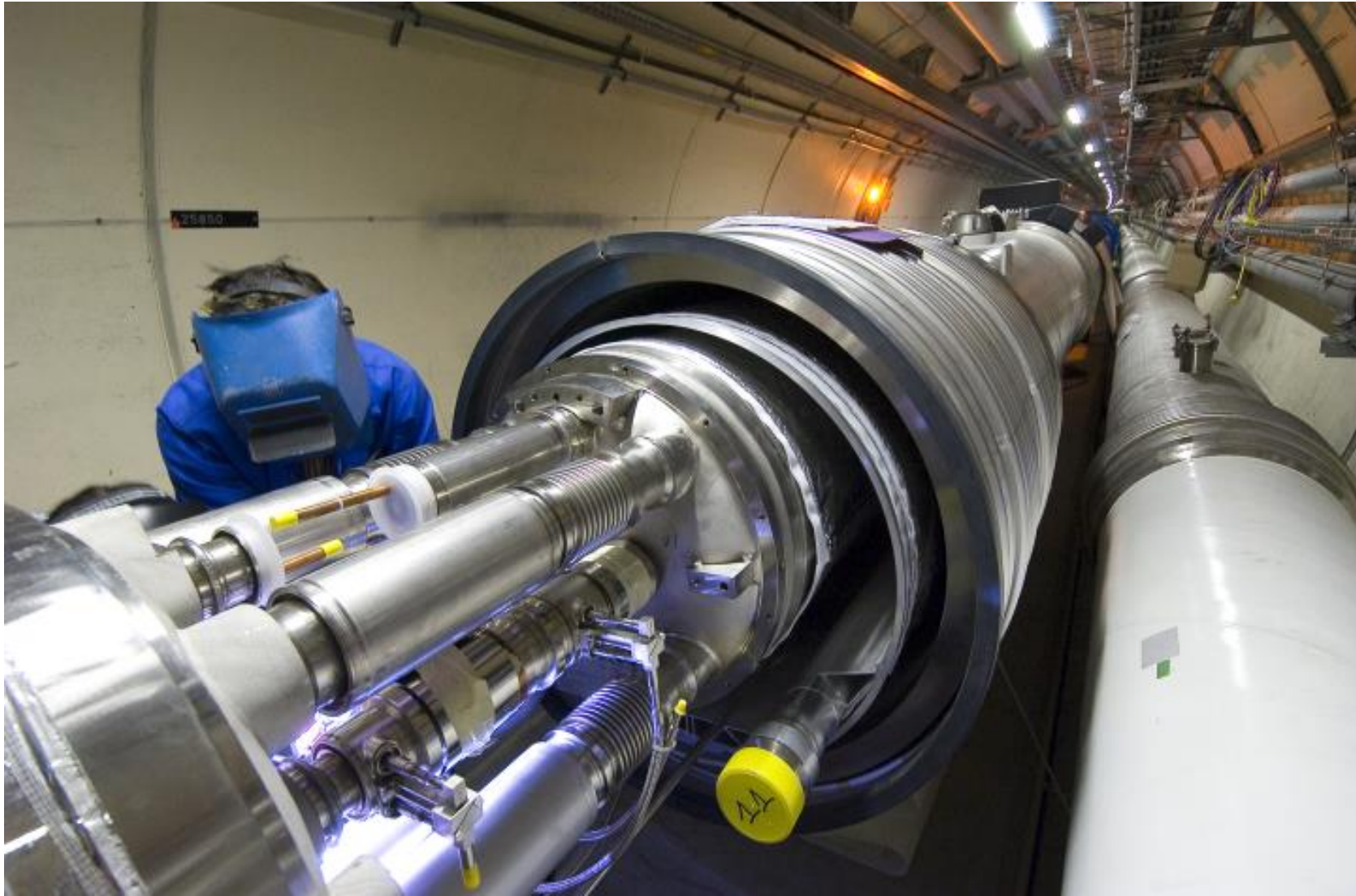




Physique et Imagerie Médicale

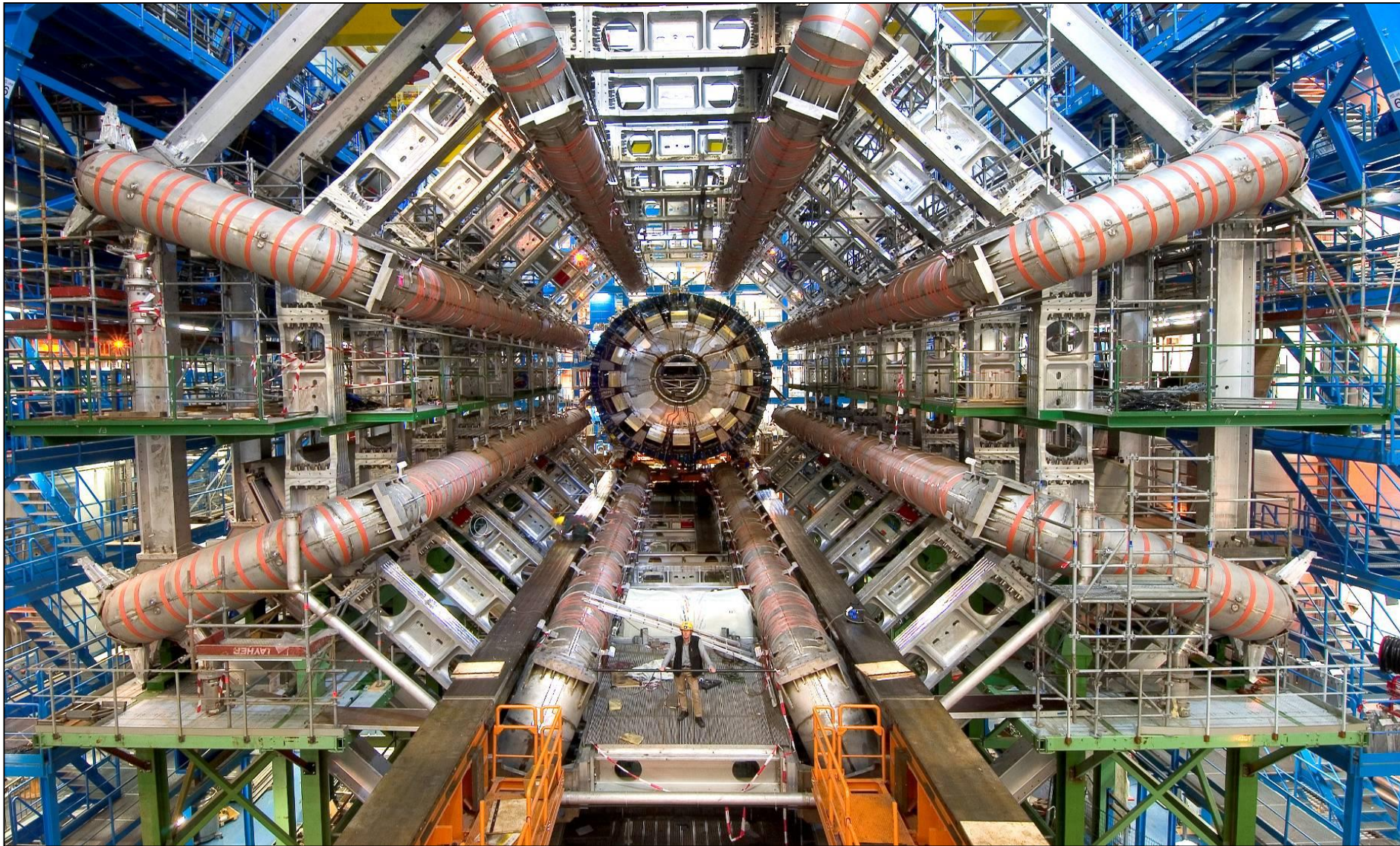
Paul Lecoq
CERN, Genève

LHC - Installation des aimants supraconducteurs (27km)

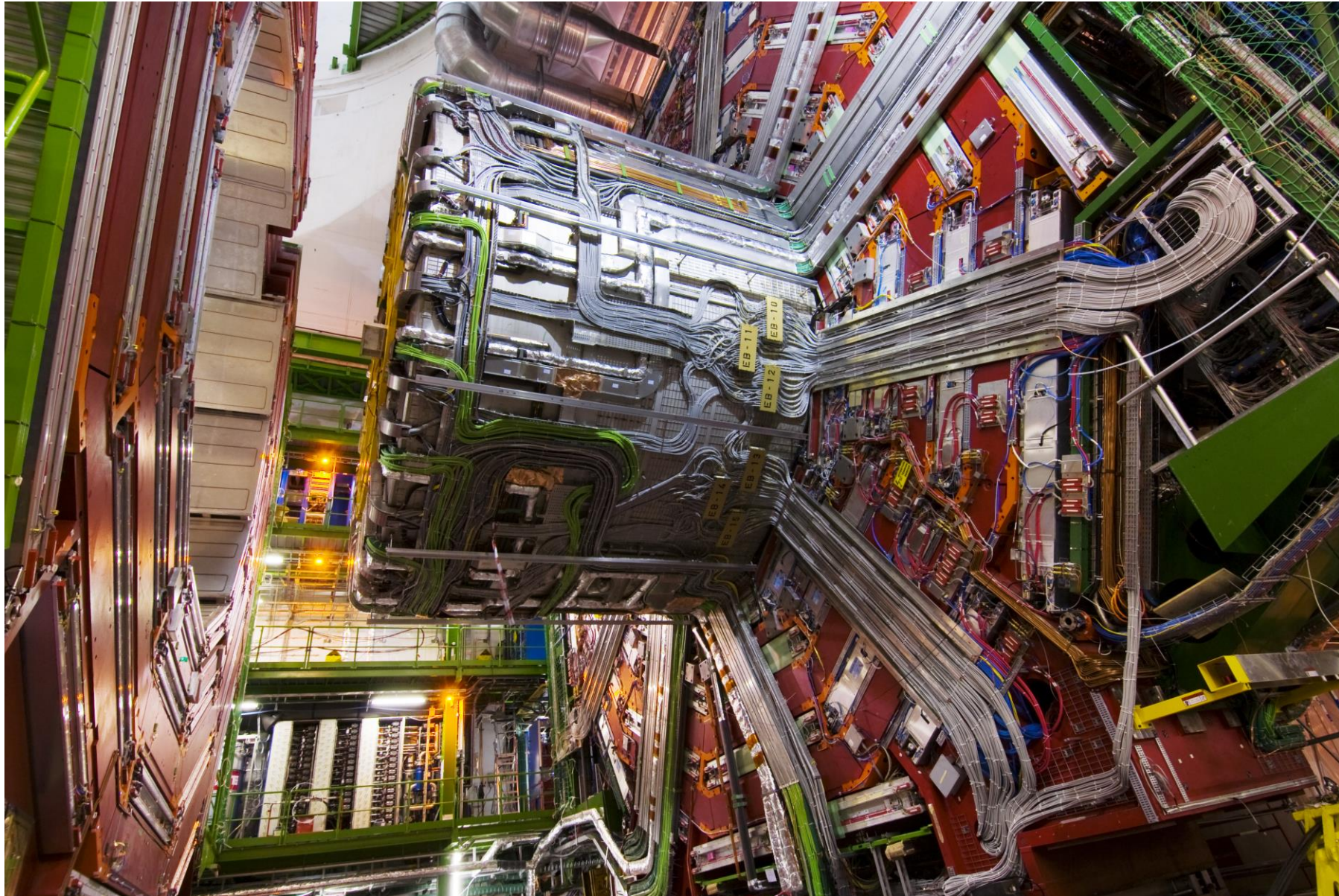




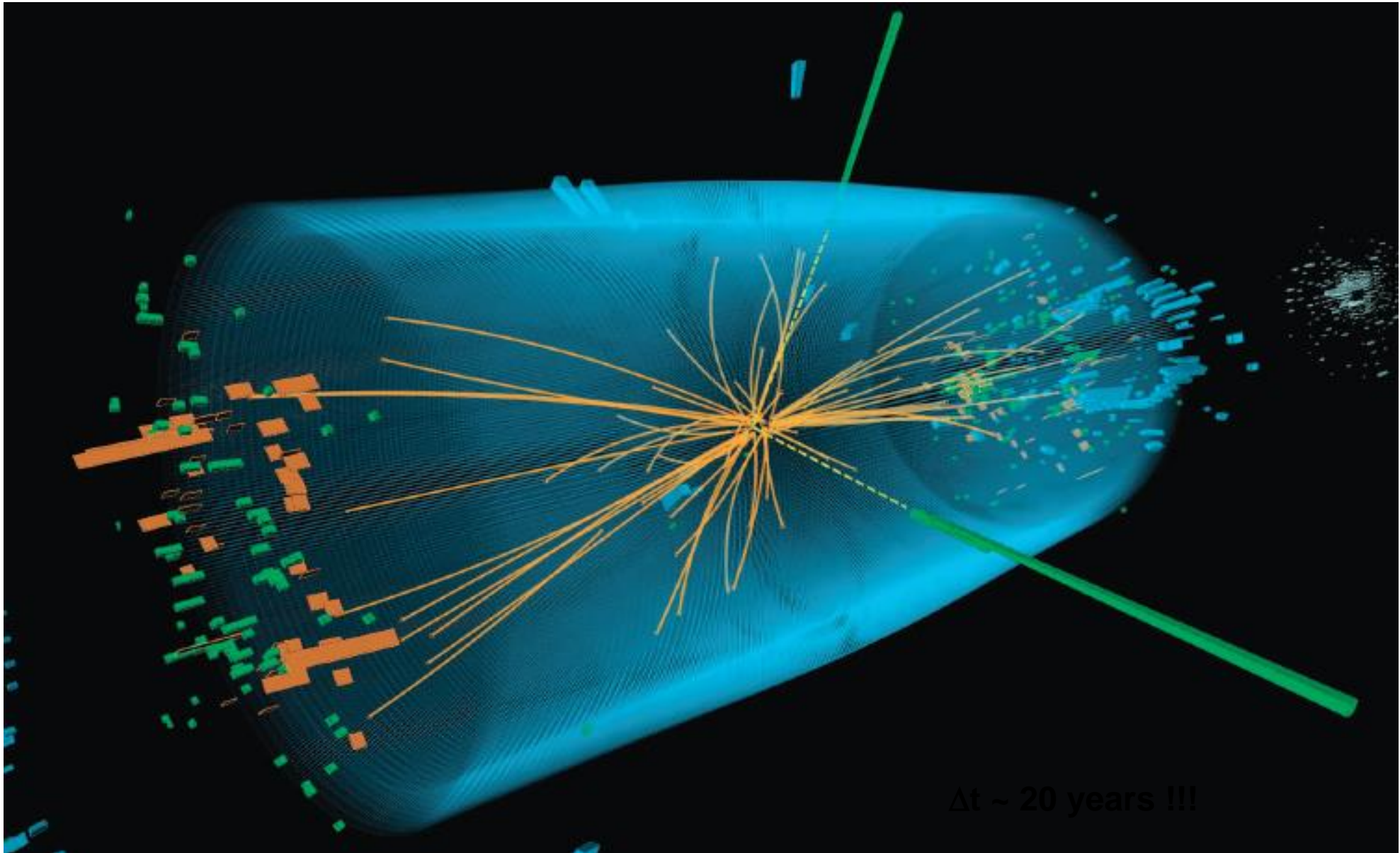
L'aimant toroidal d'Atlas



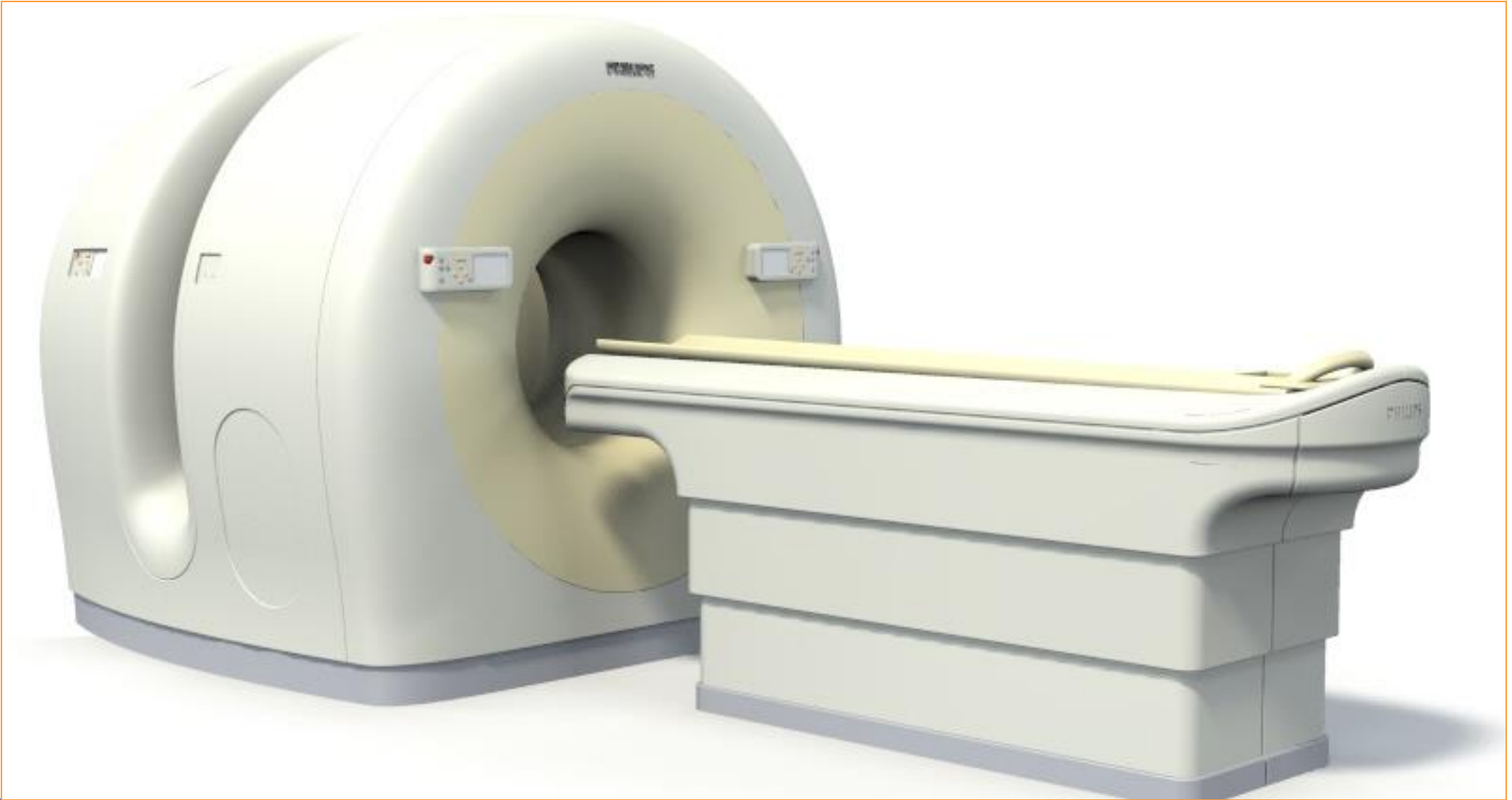
Montage de l'expérience CMS

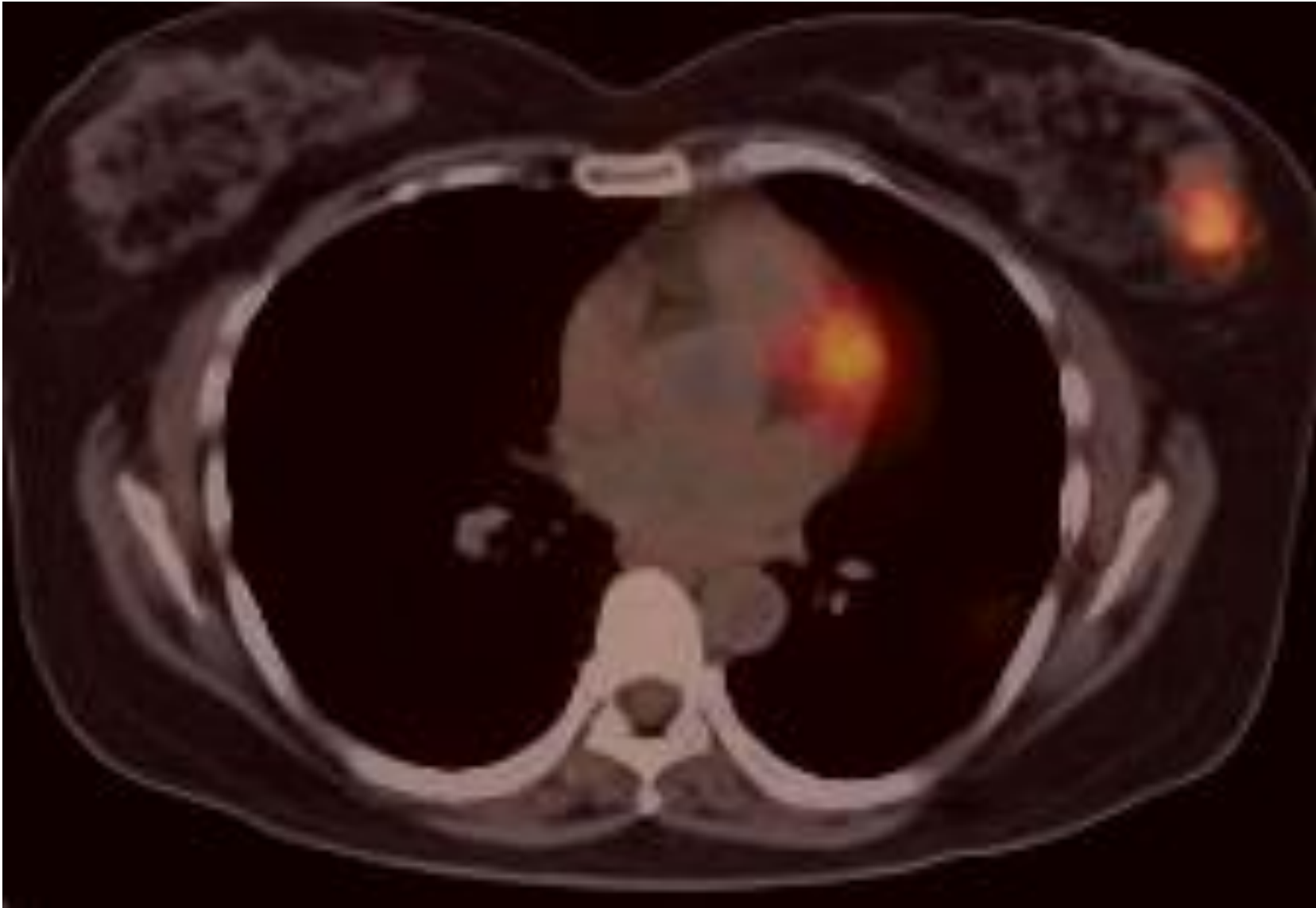


July 4, 2012 : The Higgs Boson!!



Scanner TEP/CT





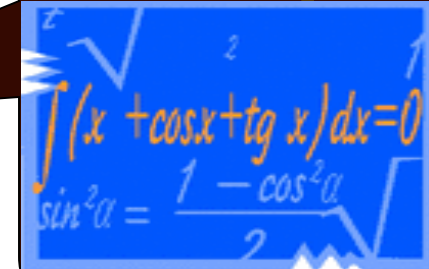
Patiente traitée
pour un cancer
du colon
révélant à
l'examen un
cancer du sein
additionnel

L'imagerie médicale: une approche pluridisciplinaire

Physique



Mathématiques



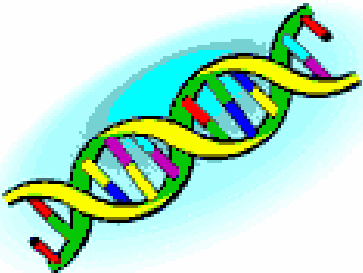
Médecine



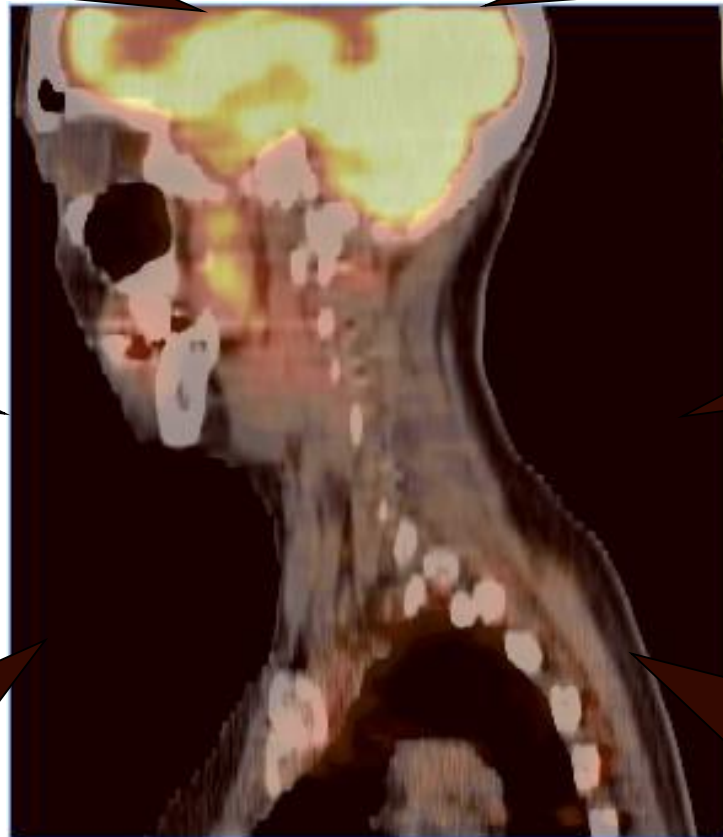
Chimie



Biologie



Informatique



La découverte des Rayons-X

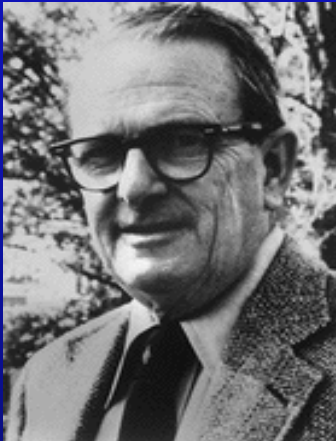
500'000'000
d'examens RX
chaque année dans le monde

- Le 8 November 1895 Röntgen découvre les Rayons X
- Le 22 November 1895 il prend le premier cliché de la main de son épouse

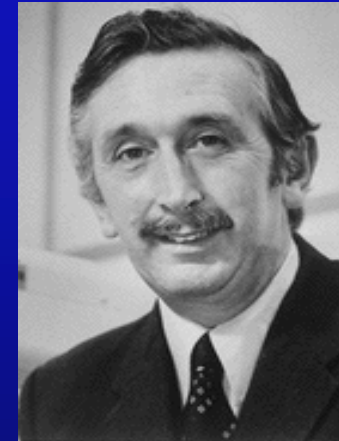
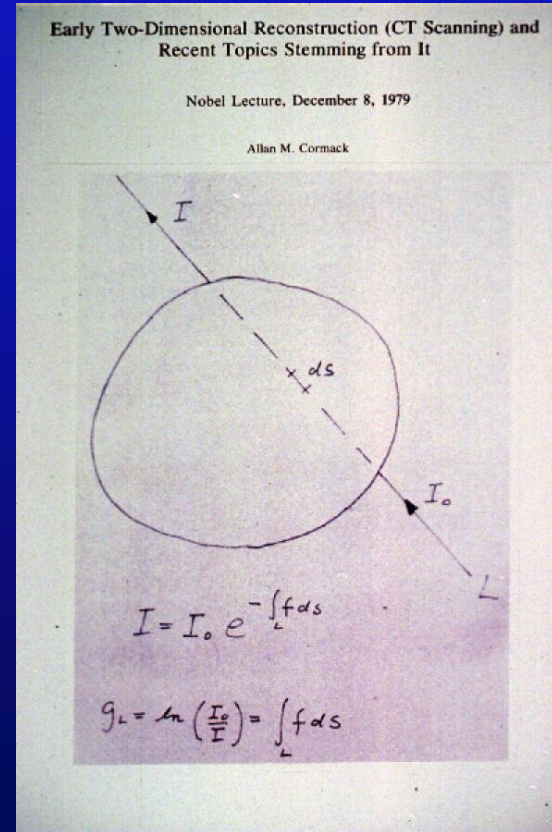


Röntgen obtient le 1^{er} prix Nobel de physique en 1901

Prix Nobel de Physiologie et Médecine 1979

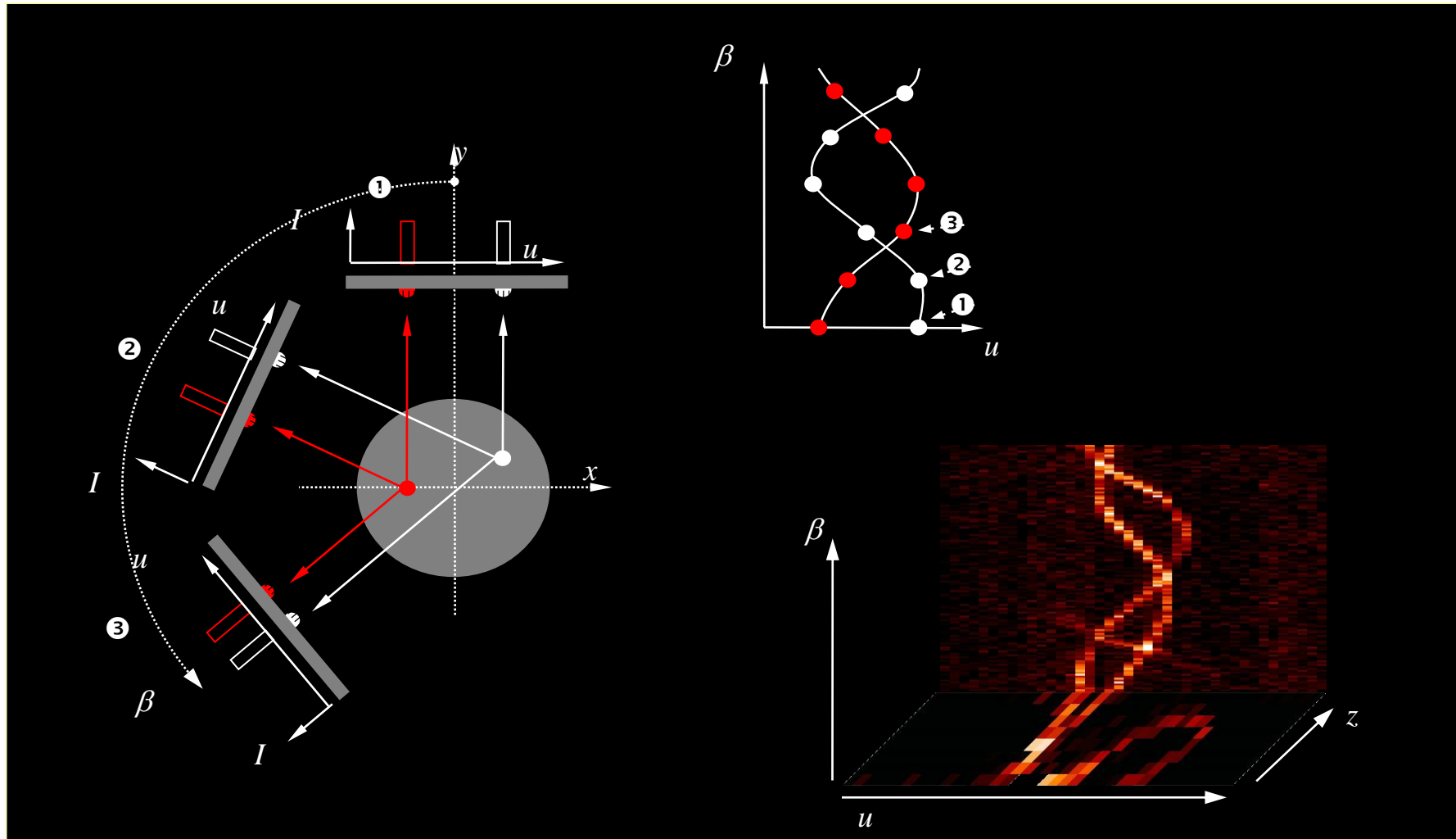


Allan MacLeod Cormack
Physicien Nucléaire
Cape Town
Harvard University
Tufts University

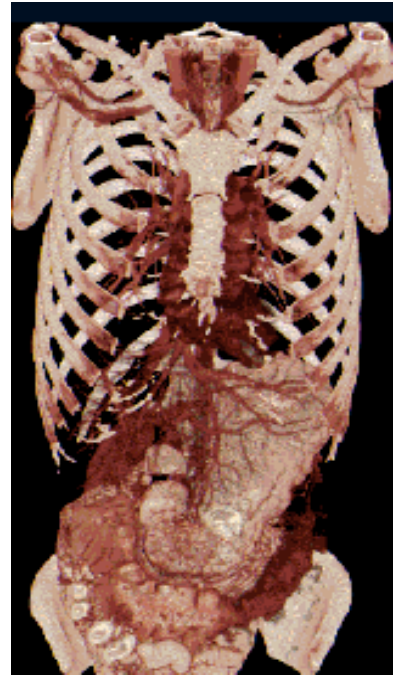
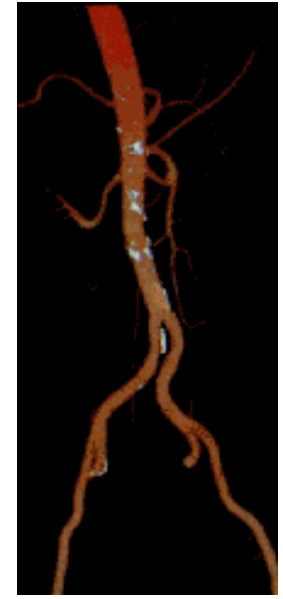
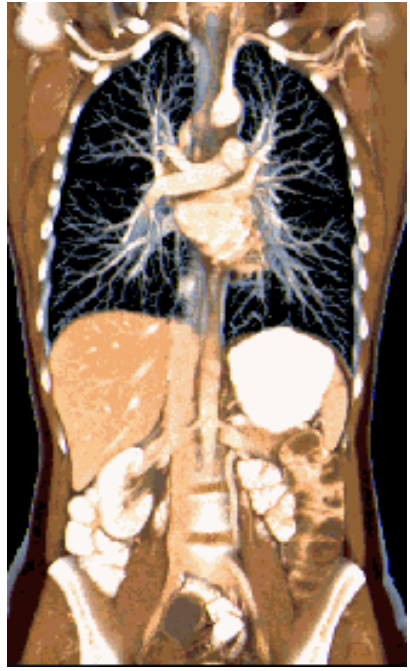


Sir Godfrey N. Hounsfield
Ingénieur électricien anglais
EMI Research

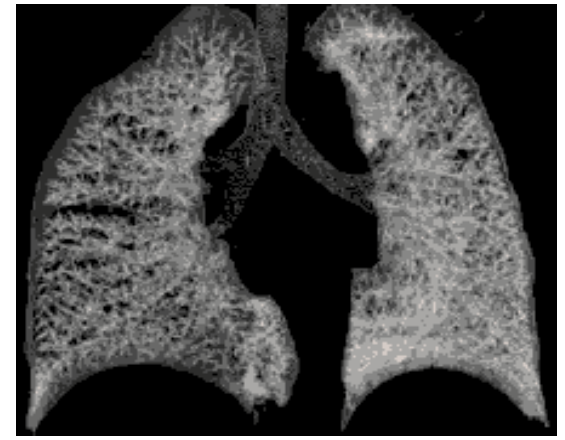
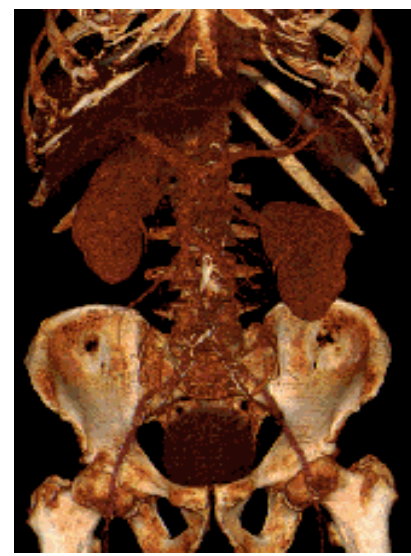
Principe de la Tomographie



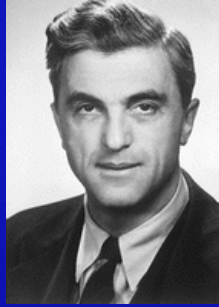
Tomographie volumétrique



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

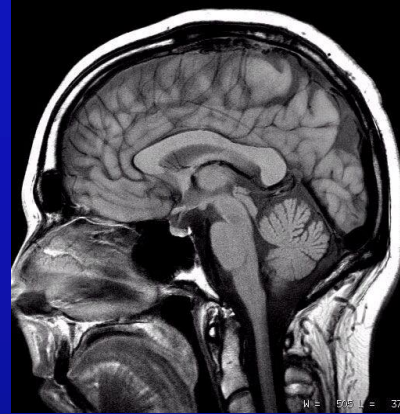






Felix Bloch
Physicien Stanford

Prix Nobel de Physique 1952

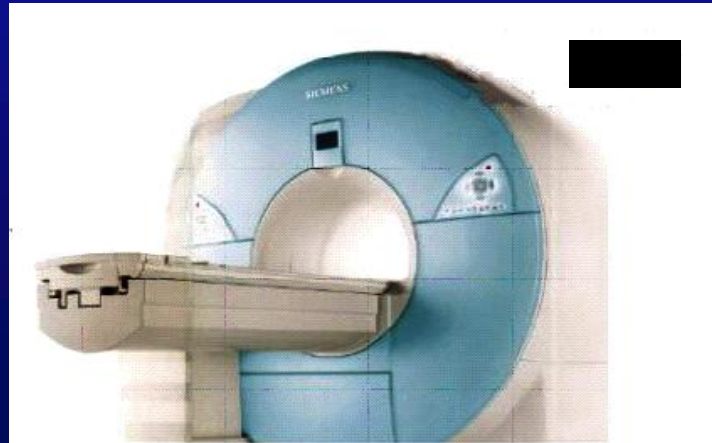


Edward M. Purcell
Physicien Harvard

Prix Nobel de Physiologie et Médecine 2003

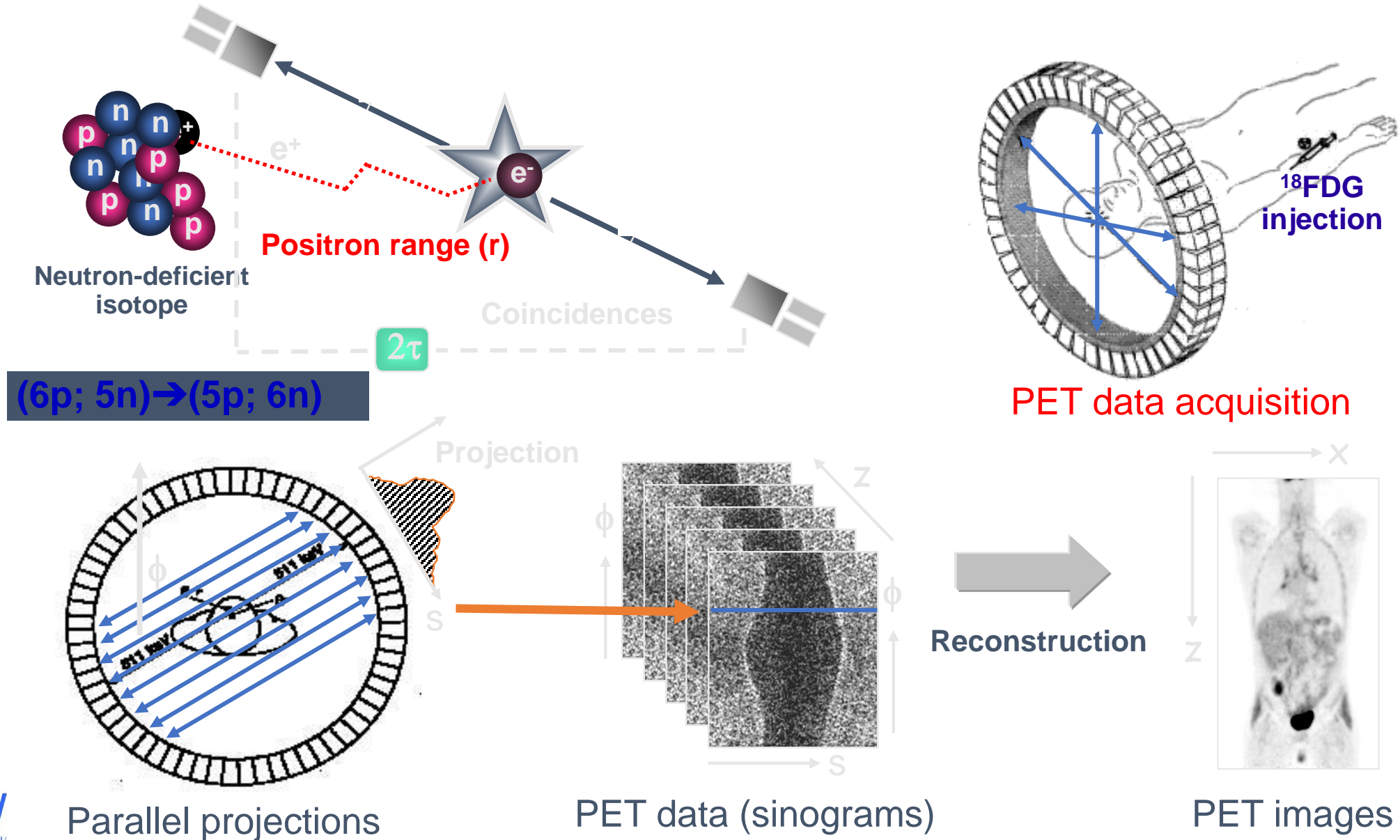


Sir Peter Mansfield
Physicien Nottingham

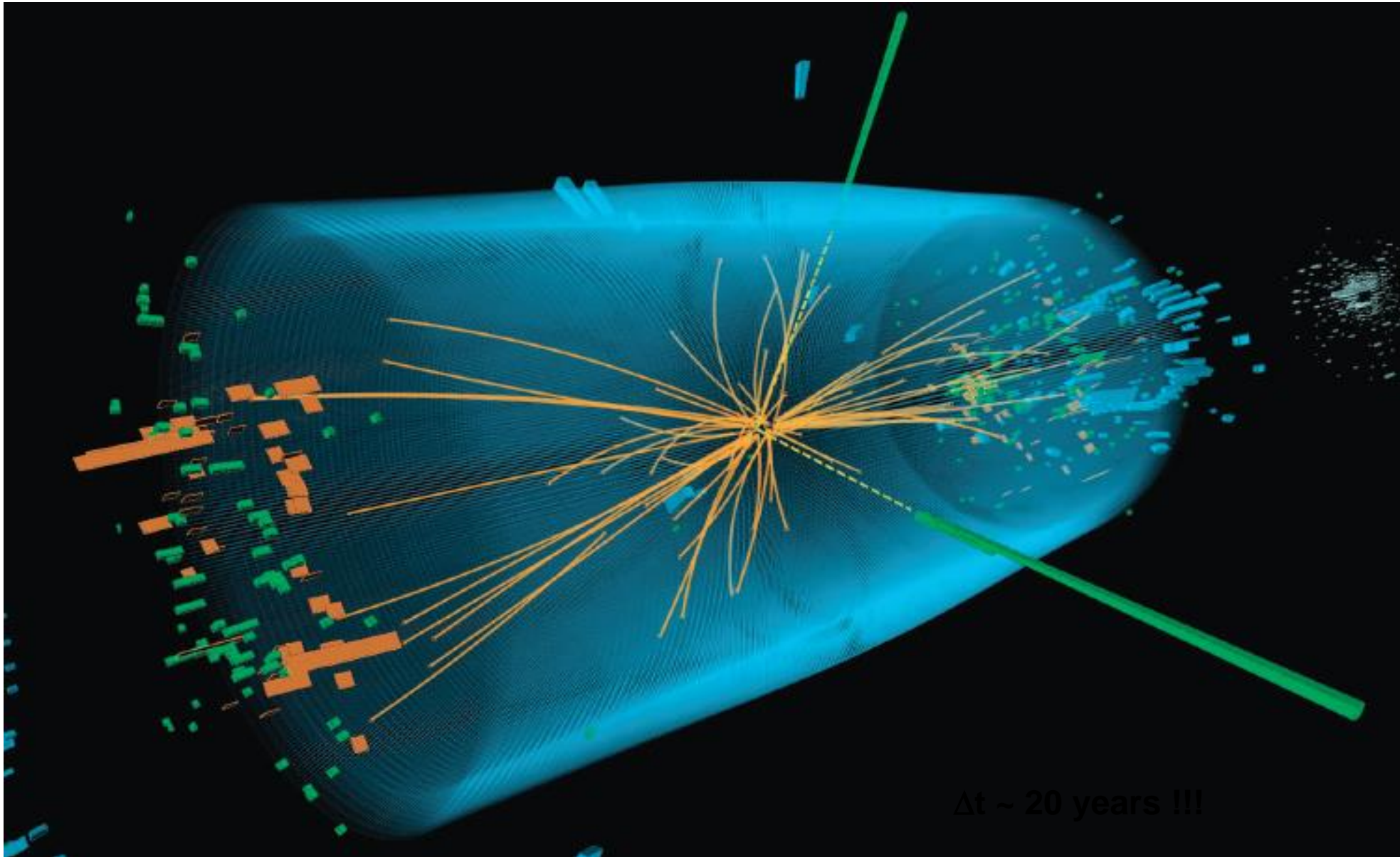


Paul C. Lauterbur
Chimiste Uni. Illinois

Imagerie par émission de positron (TEP)



July 4, 2012 : The Higgs Boson!!



The PET World Picture







Need to Image
0.000000511 TeV*
Photons

*511 keV

Signal Levels Are Very Low

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

Cahier des charges pour la physique

- 1. Cristaux** Transfert technologique 
 - Densité élevée ($> 6 \text{ g/cm}^3$)
 - Emission rapide ($< 100 \text{ ns}$), spectre visible
 - Emission lumineuse modérée à élevée
 - Excellente résistance aux radiations
- 2. Photodétecteurs** Transfert technologique 
 - Compact
 - Grande efficacité quantique et gain élevé
 - Grande stabilité
- 3. Electronique de lecture** Transfert technologique 
 - Mise en forme rapide du signal, faible bruit
 - Fortement intégrée
- 4. Architecture d'acquisition DAQ** Transfert technologique 
 - Intégrée et parallèle, temps mort réduit
- 5. Logiciels** Transfert technologique 
 - Simulation précise par Monte Carlo
- 6. Intégration** Transfert technologique 
 - Systèmes compacts avec un très grand nombre de canaux ($> 10'000$)

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

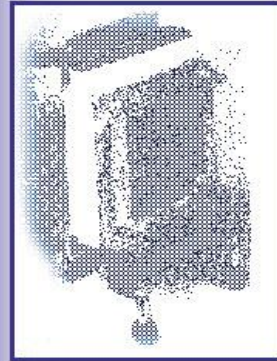
1977

when PET started at CERN

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

TOMOGRAM

RECONSTRUCTION



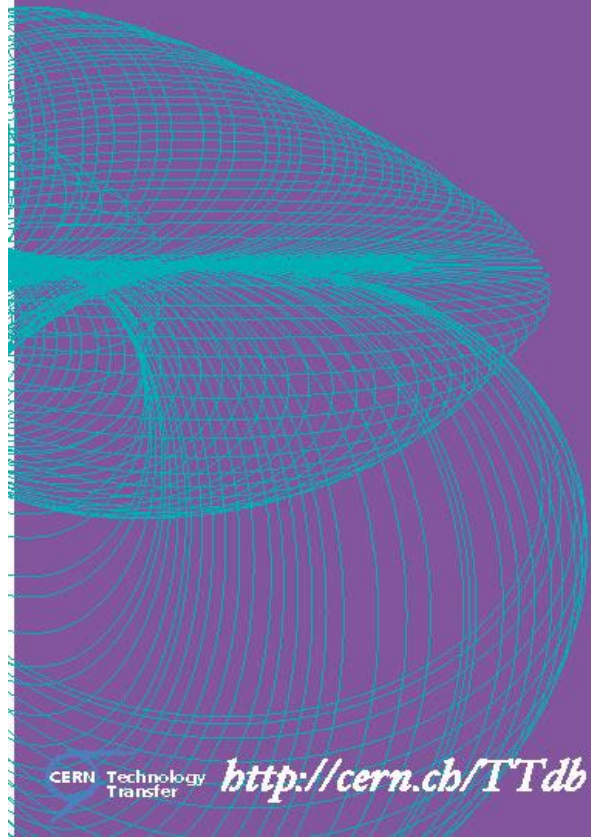
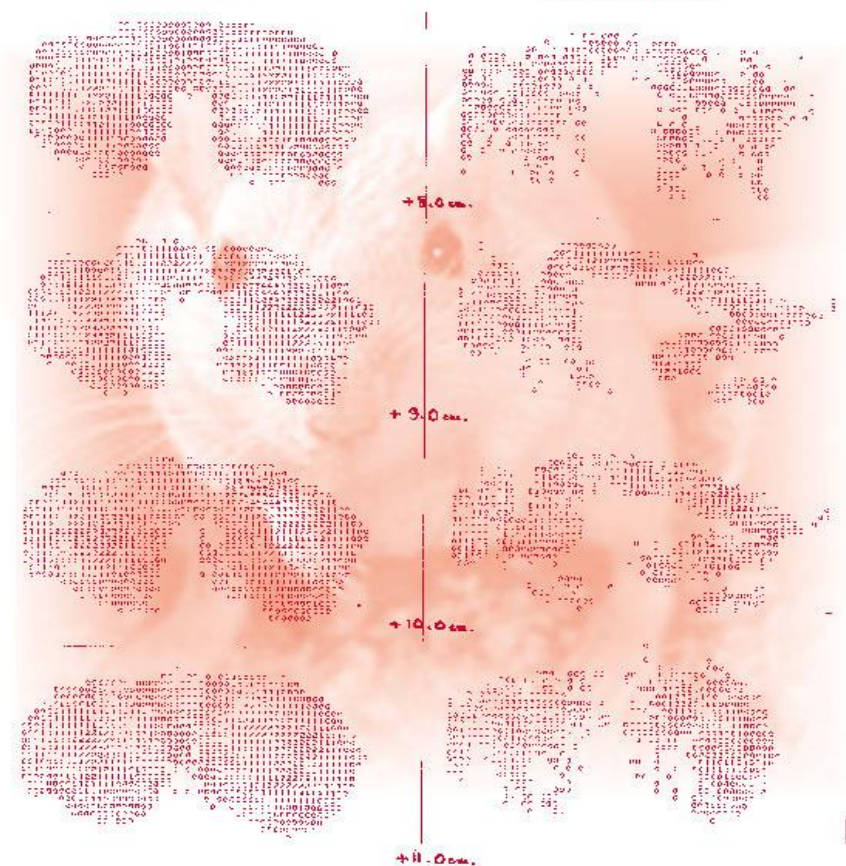
(Jeavons, Townsend et al)

Spatial resolution 2.4 mm FWHM

Maximum data rate: 3000 c.p.s

Sensitivity: 25 c.p.s/ μCi

1 μCi $\approx 3.7 \cdot 10^4 \text{Bq}$



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

Invention of the PET/CT

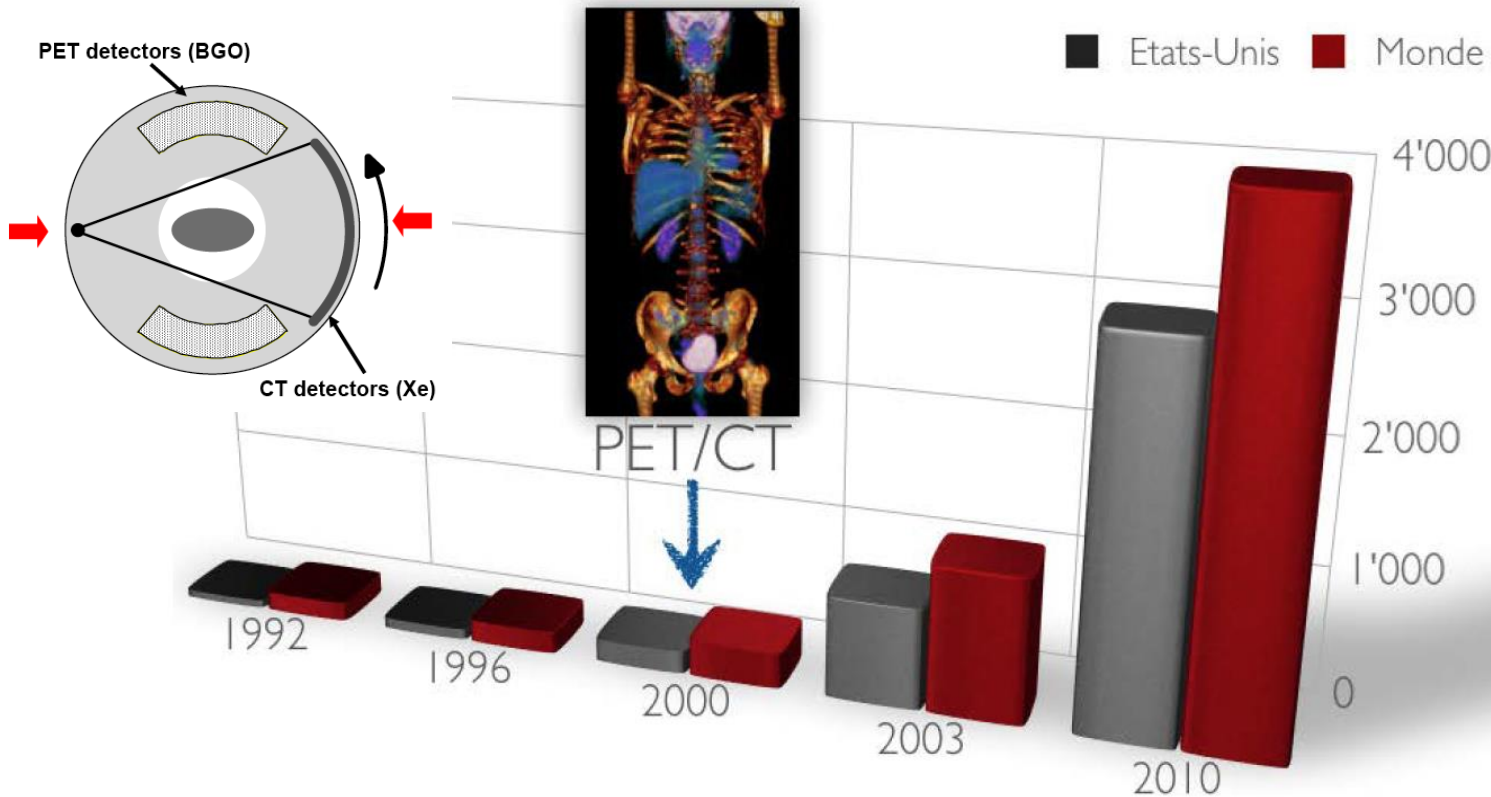
PET/CT



TIME
DECEMBER 4, 2000

Time Magazine's
Medical Invention
of the Year 2000

Disruptive Technology

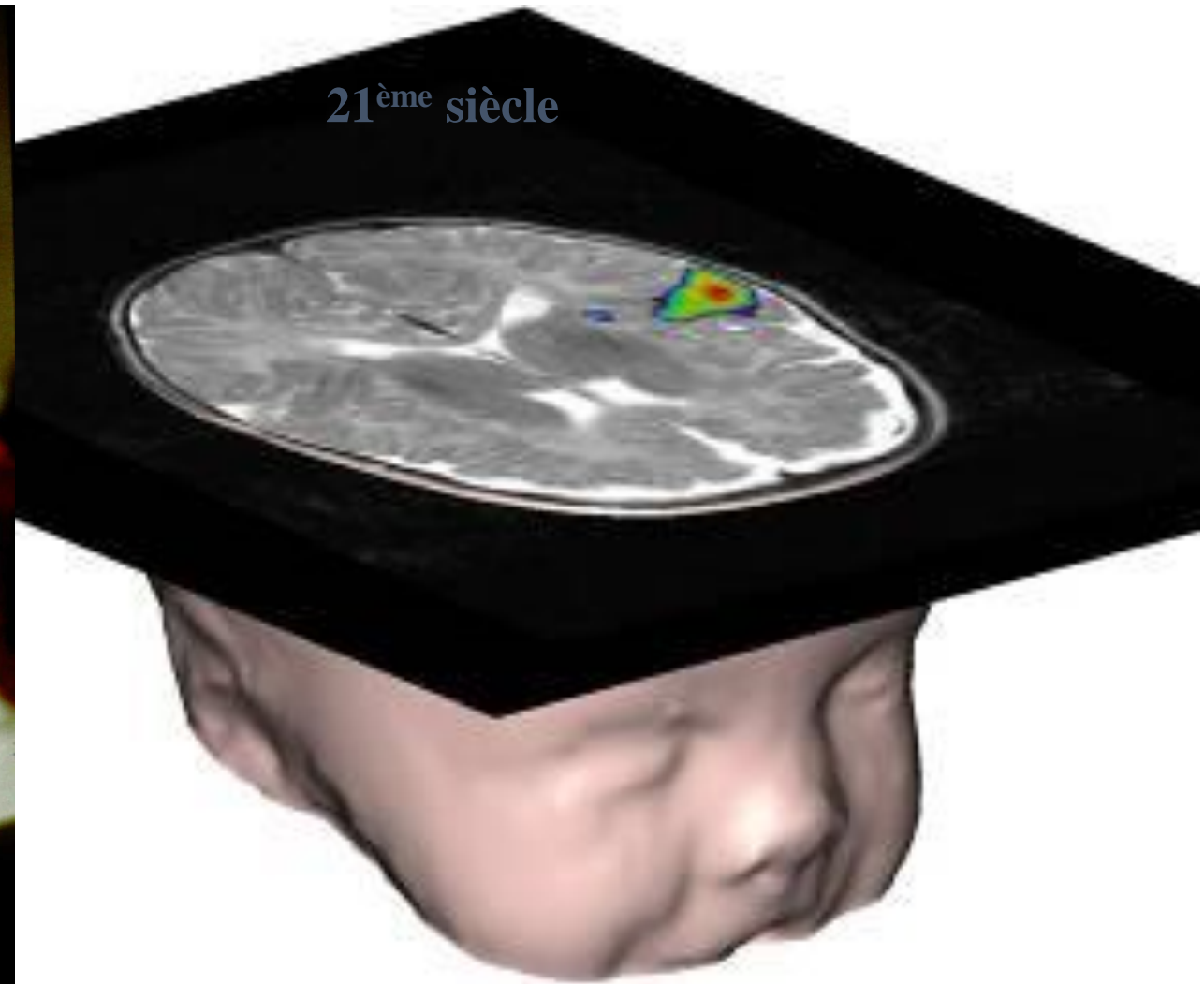


PET/CT Invention



David Townsend
(former CERN)

Petite histoire résumée de l'imagerie in-vivo



Differents types d'imagerie pour différents types d'information

- Imagerie anatomique
 - Localiser des masses ou des lésions
 - *Optique, CT, ultrasons, IRM*
- Imagerie fonctionnelle
 - Quantifier des modification dynamique du métabolisme au niveau des organes
 - *Ultrasons (Doppler), IRM (Bold), Imagerie nucléaire (PET/SPECT)*
- Imagerie cellulaire
 - Etudier les échanges entre cellules entre elles, et avec leur environnement (stroma)
 - *Optique, IRM, Imagerie nucléaire (PET/SPECT)*
- Imagerie moléculaire
 - Etudier les chemins moléculaires impliqués dans la production de protéines, d'enzymes, différents métabolites (sucres, acides aminés, acides gras, etc...)
 - *Imagerie nucléaire (PET/SPECT)*

Molecular Imaging in Medicine & Biology

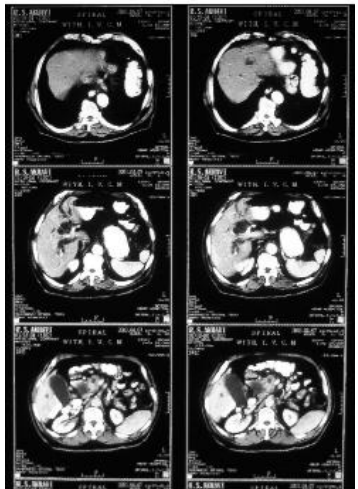
□ Molecular Imaging to answer challenge of modern biology

- 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**

Imaging Modalities



CT

A Tissue Density, Z
20-50 μm

Ultrasound



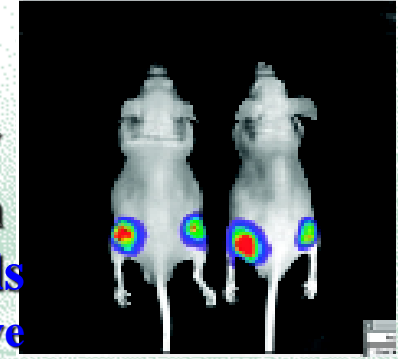
A **F**

Structure
0.1 mm
Doppler

Optical (Bioluminescence, fluorescence)

A **M**

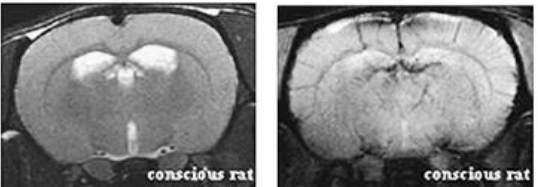
Topography
 μm to mm
 $\sim 10^3$ cells
 \neq quantitative



Photons involved

4.7T, Dual Coil, Coil, T1 Weighted SE

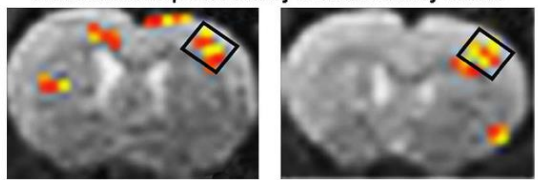
4.7T, Dual Coil, T2 Weighted GE



conscious rat

conscious rat

Activational Maps of Primary Somatosensory Cortex



MRI

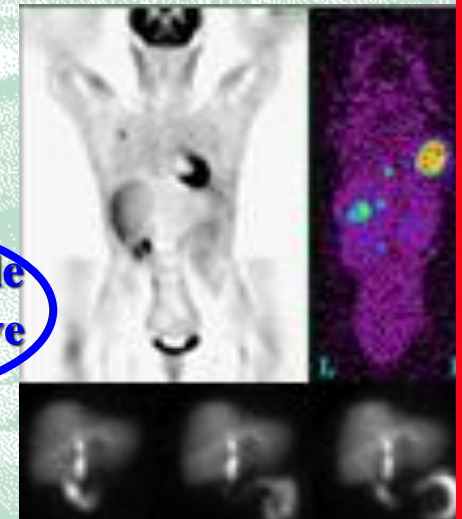
A **F** **M**

H Concentration
0.1 mm
BOLD, DCE
 β -galactocidase
0.1 $\mu\text{mole H} / \mu\text{mole } ^{31}\text{P}$

PET/SPECT

F **M**

Radiotracer
 $\sim 1\text{-}2$ 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 métastatique
- Optimiser l'action thérapeutique en fonction du génotype du patient
- Evaluer instantanément l'efficacité du traitement

*Implique une nouvelle génération
de systèmes d'imagerie*

Médecine personnalisée

Approche globale

Médecine personnalisée



Un diagnostic



Un traitement



Diagnostic moléculaire



Imagerie moléculaire

+ Génomique

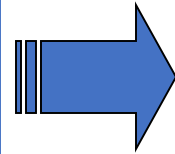


Traitement individualisé

L'imagerie: quelle qualité pour voir quoi et dans quelles conditions?



- Voir des lésions plus petites
- 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
- Rapport Signal/Bruit
- Sensibilité

Etudes de plus en plus spécifiques sur modèles animaux

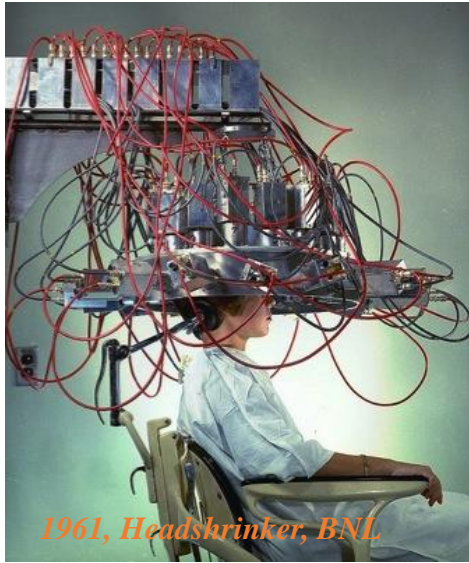
- L'imagerie petit animal se fait généralement sous anesthésie
- L'anesthésie modifie les fonctions cervicales et biaise les études neuro-physiologiques
- RATCAP, développé à BNL est un TEP miniaturisé et portable pour animal éveillé
- 12 blocs de 4x8 cristaux de LSO $2 \times 2 \times 5 \text{ mm}^3$ 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

Organ-specific imaging devices: brain



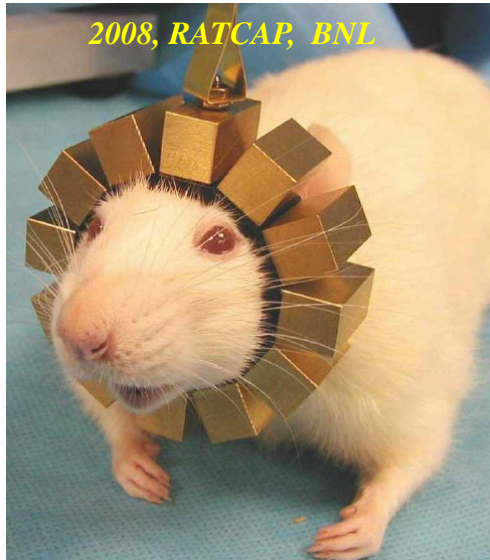
1961, Headshrinker, BNL



2011, PETHAT, Hamamatsu



2013, BrainPET, Hamamatsu



2008, RATCAP, BNL

2012, HELMETPET, Majewski



2015, HELMET CHIN, Yamaga



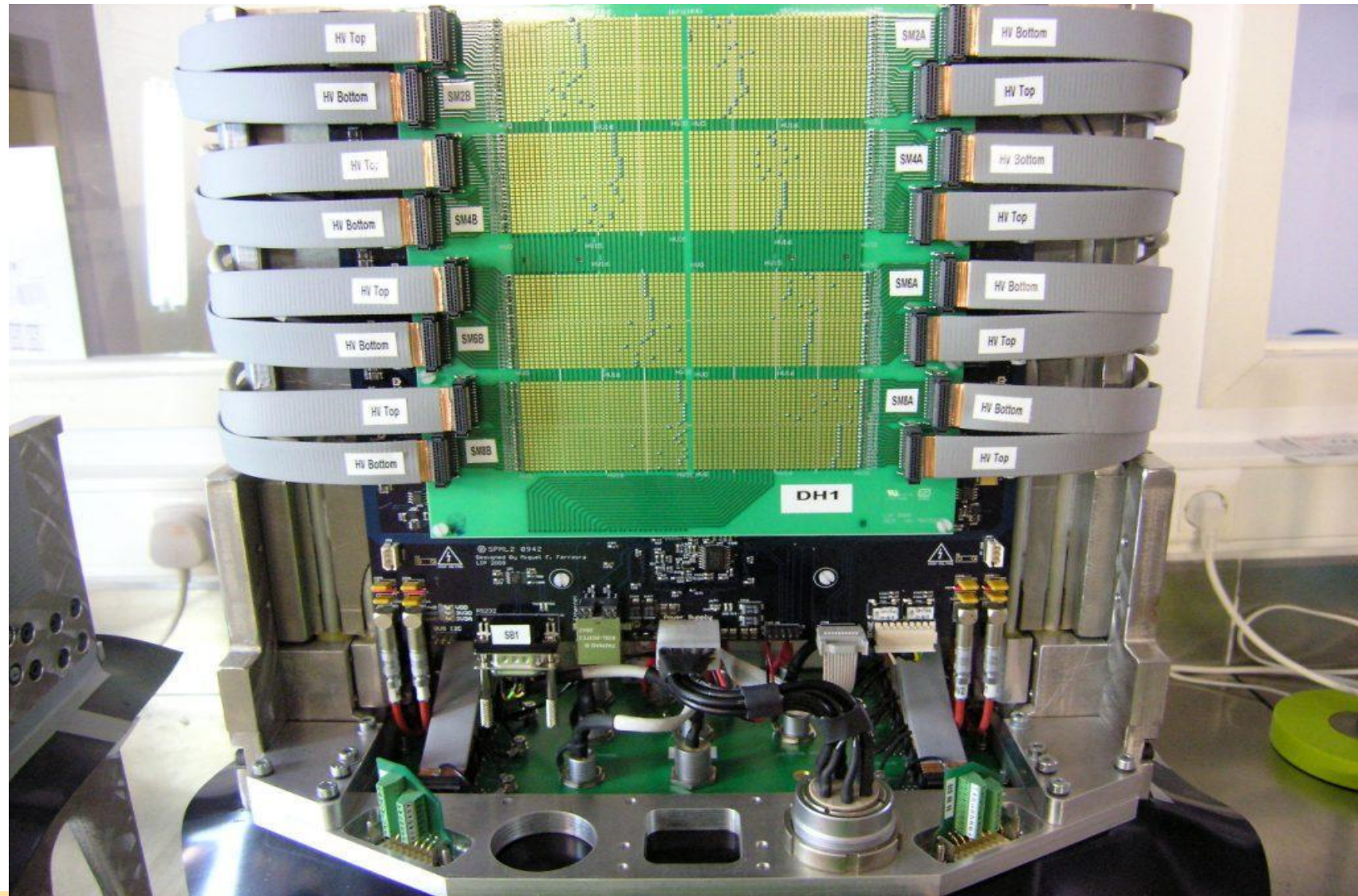
Courtesy: S. Majewski, West Virginia University

ClearPEM-Sonic a collaborative project between physicians and physicists



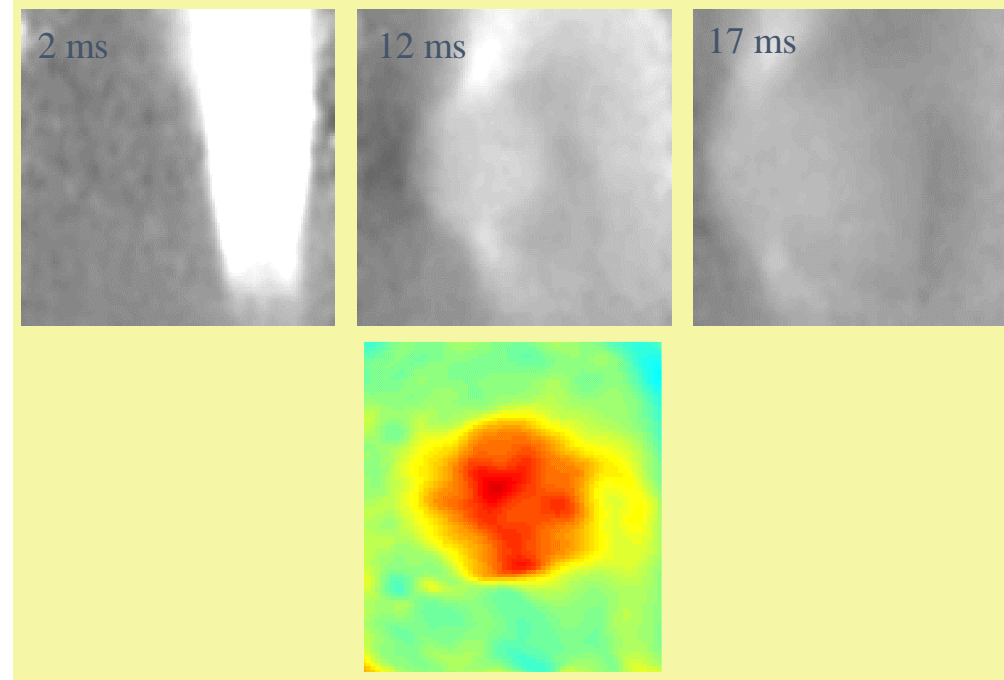
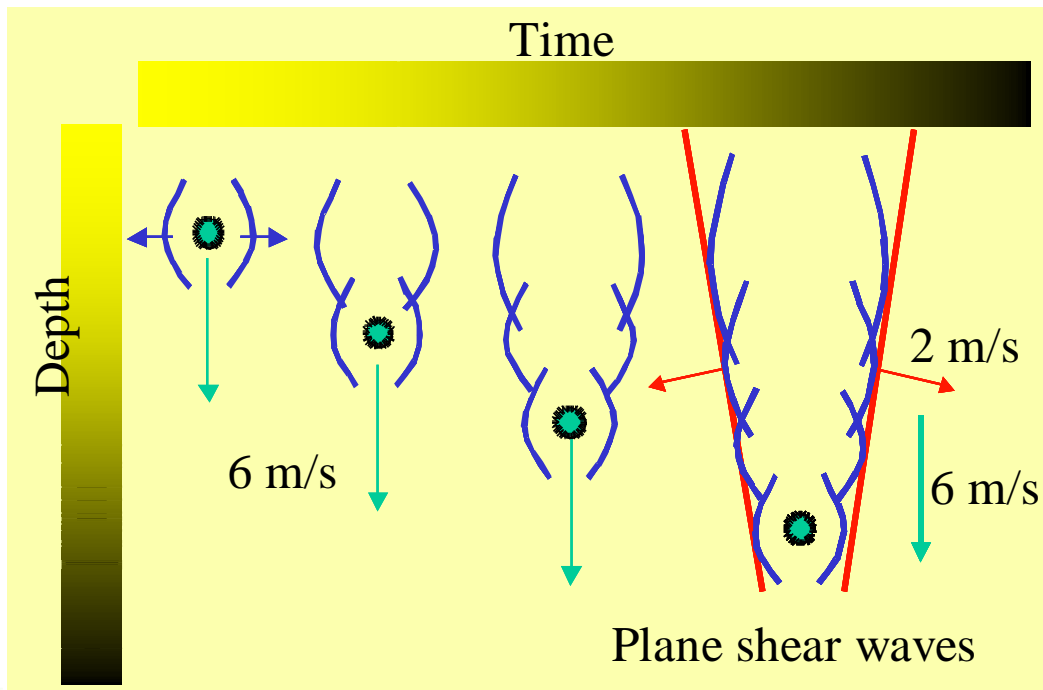
Objective: Detect 3mm tumors and define their cancerous status

Des technologies d'avant-garde: ClearPEM

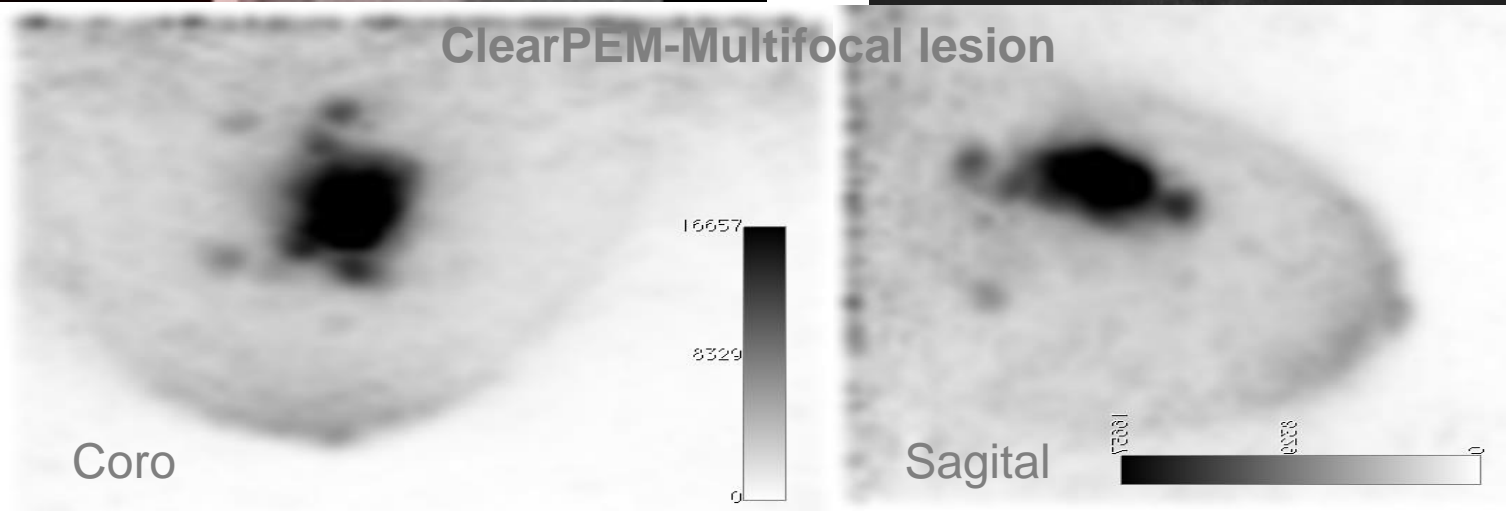
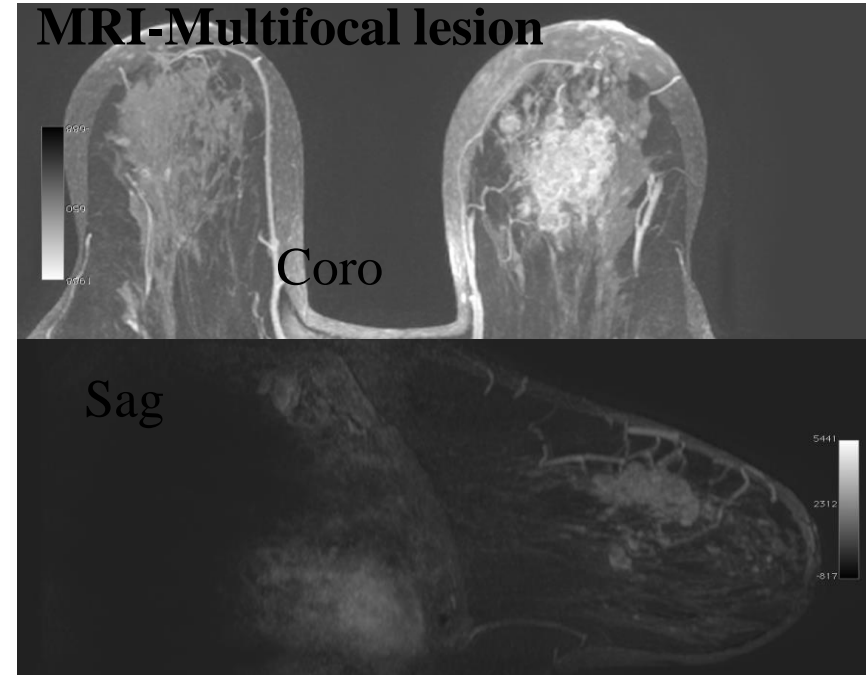
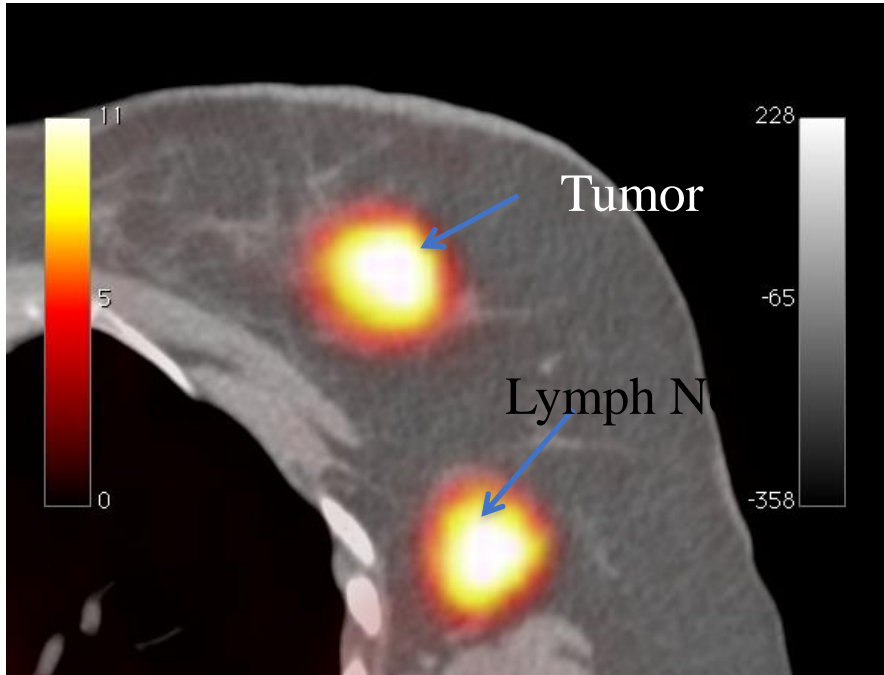


Des technologies d'avant-garde: Ultrasons

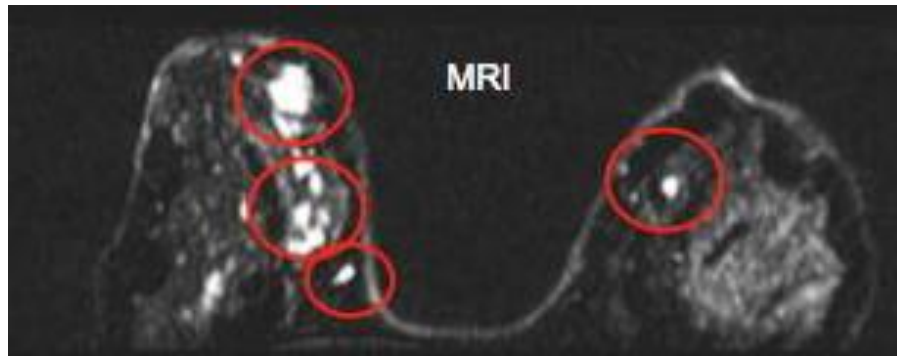
- Focus ultrasound beam in tissue
- Propagate focal point at a supersonic speed in breast
- Measure the deformation of the shock wave by a tumor



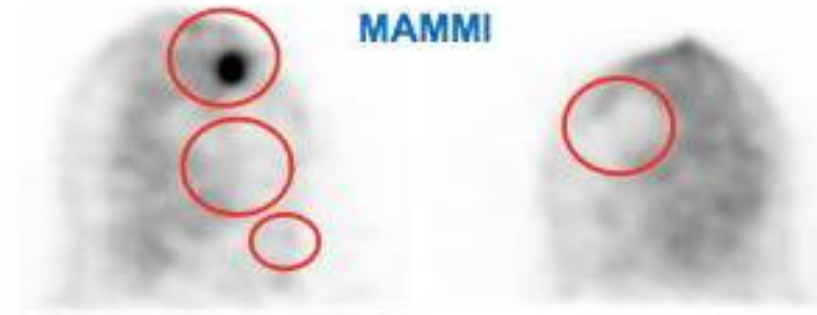
Benefit of dedicated breast PET imaging



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

Increasing effective PET sensitivity

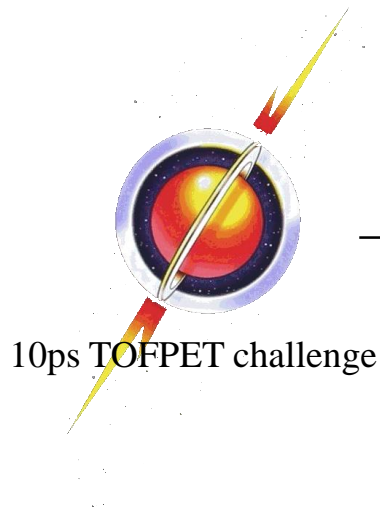
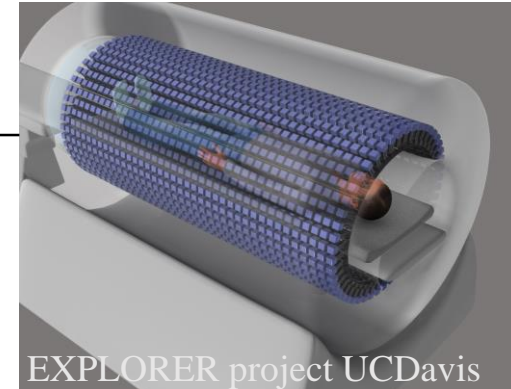
- PET is the imaging modality with the highest sensitivity, at the picomolar level
- New medical challenges require a significant sensitivity increase
 - Tracking small number of cells
 - Stem cells biodistribution and differentiation studies
 - Immune cells tracking for immunotherapy
 - Precise pharmacodynamic studies
 - Dose reduction and opening PET scans to new categories of patients (pregnant women, children, foetus)

Increasing effective PET sensitivity



- Improve detector efficiency

- Increase solid angle coverage



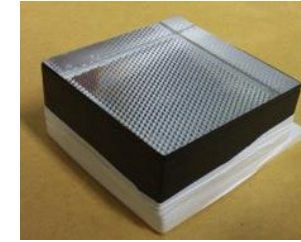
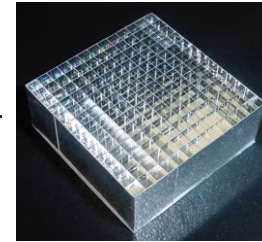
- Improve timing resolution

Improve detector efficiency

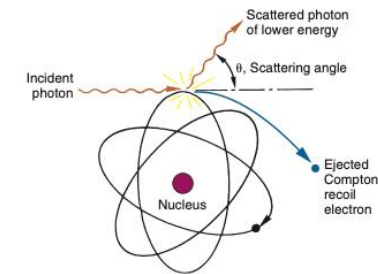
- Higher stopping power materials



- Improved packing fraction



- Better handling of Compton scatter

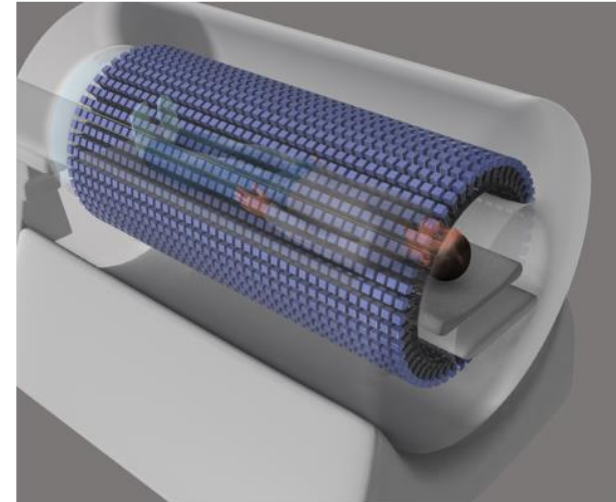
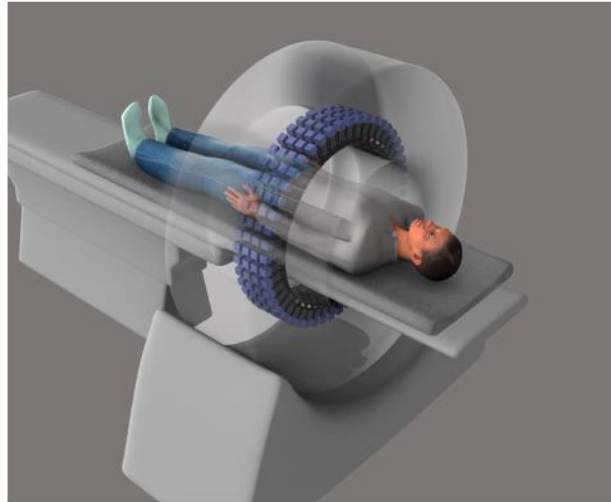


Gain of **~1.4 to 2 fold** achievable

Improve solid angle coverage

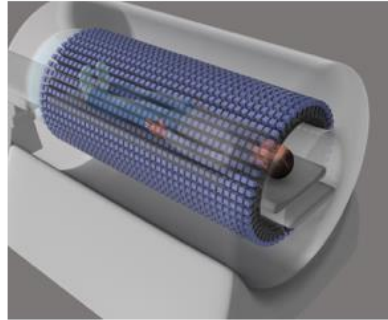
- Increase solid angle coverage

The **EXPLORER** project



~40-fold increase for total-body imaging

The Future of EXPLORER



2m long scanner



100ps CTR



- Higher stopping power materials
- Improved packing fraction
- Better handling of Compton events

Effective
Sensitivity
Gain

40

X

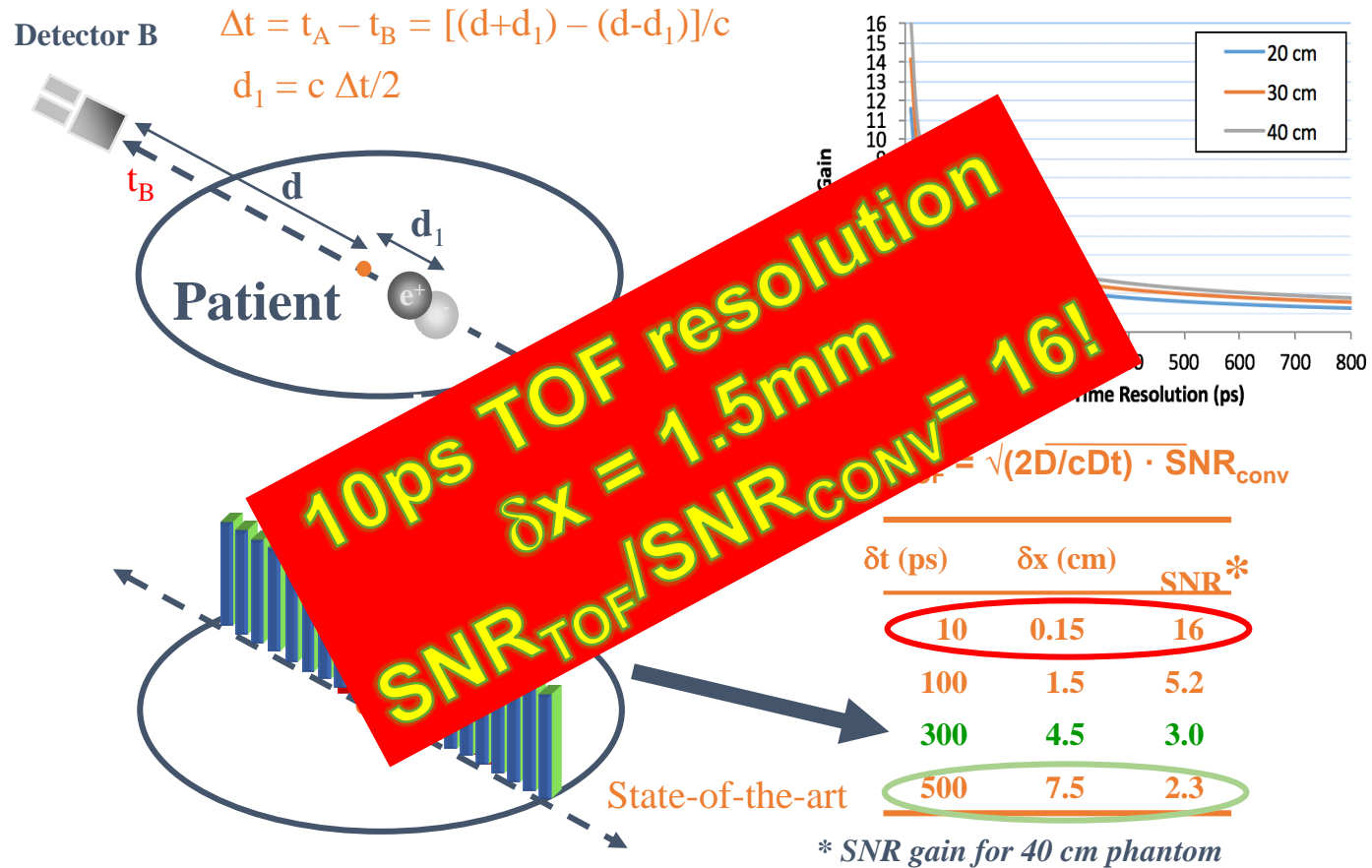
5

X

2

= ~400

Improve Timing Resolution



Sensitivity gain via Timing Resolution



- Improve timing resolution
 - Gain proportional to $1/\Delta t$
 - TOFPET with 10ps timing resolution would result in a **~200 fold** sensitivity gain /non TOFPET
 - **~20 fold** sensitivity gain /Biograph Vision

IEEE TRANSACTIONS ON RADIATION AND PLASMA MEDICAL SCIENCES, VOL. 1, NO. 6, NOVEMBER 2017

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Pushing the Limits in Time-of-Flight PET Imaging

P. Lecoq[©], Fellow, IEEE

- **> 15-fold improvement in SNR**

- Reconstruct at higher spatial resolution
- Detect smaller lesions
- Detect low-grade disease
- Better statistics for kinetic modeling



Conventional PET



10ps TOFPET

Adapted from S. Cherry, UC Davis

Image Longer

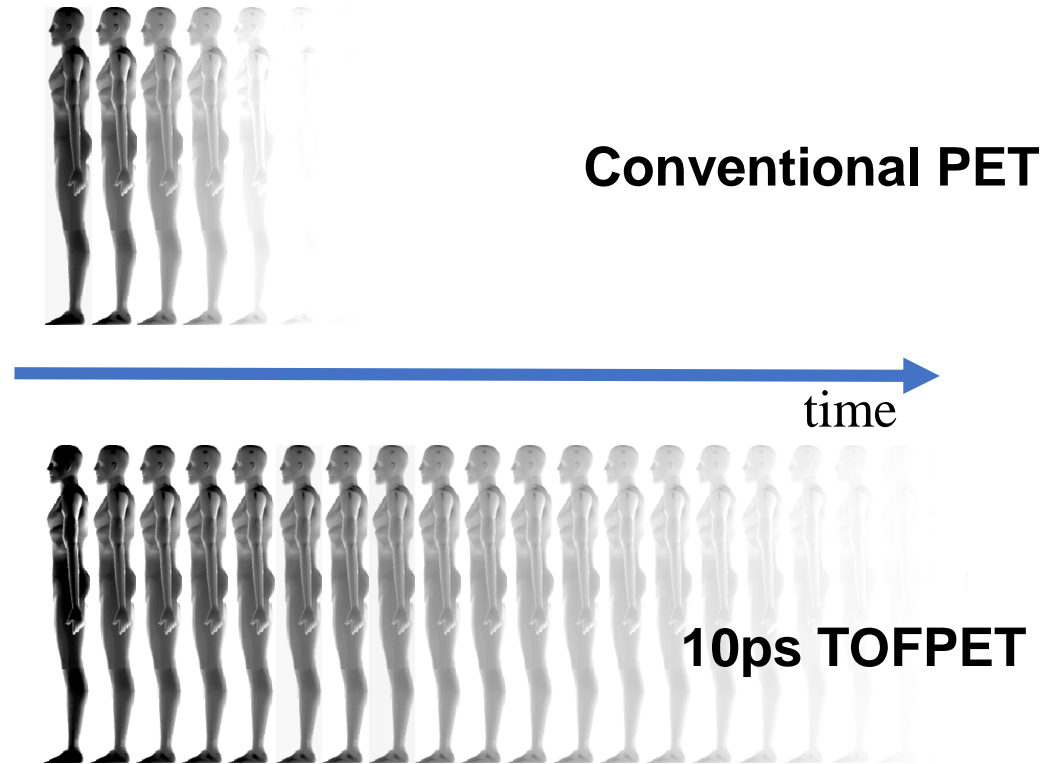
- **200-fold greater dynamic range**

can image for seven more half lives

- **^{11}C**
Up to 4 hours

- **^{18}F**
Up to 20 hours

- **^{89}Zr**
Over 30 days



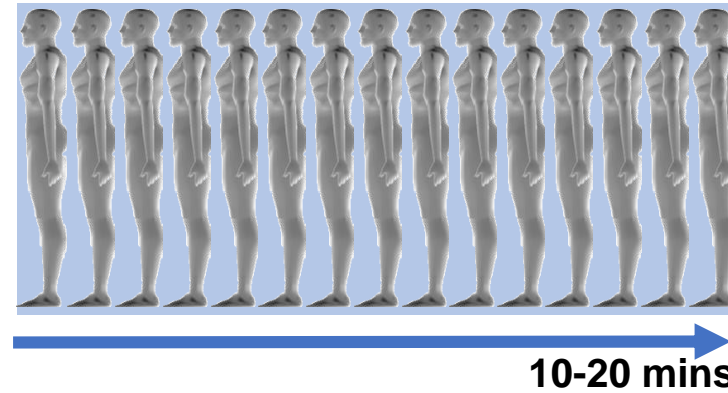
Adapted from S. Cherry, UC Davis

10ps TOFPET

5 seconds/bed position

- Image in a single breathhold
- Reduce respiratory/cardiac/bolus motion
- Higher resolution
- Total-body kinetic imaging with high temporal resolution

Conventional PET

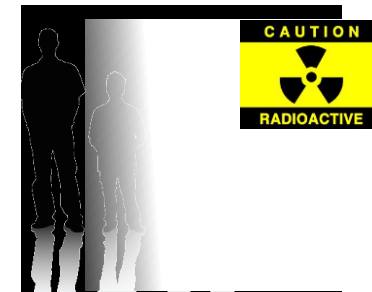


**10ps TOFPET
< 30s**

Image Gently (Low Dose)

- **200-fold reduction in dose**

- Whole-body PET at ~ 0.03 mSv
- Annual natural background is ~ 2.4 mSv
- Return flight (SFO-FRA) is ~ 0.11 mSv
- PET can be used with minimal risk – new populations



Conventional PET



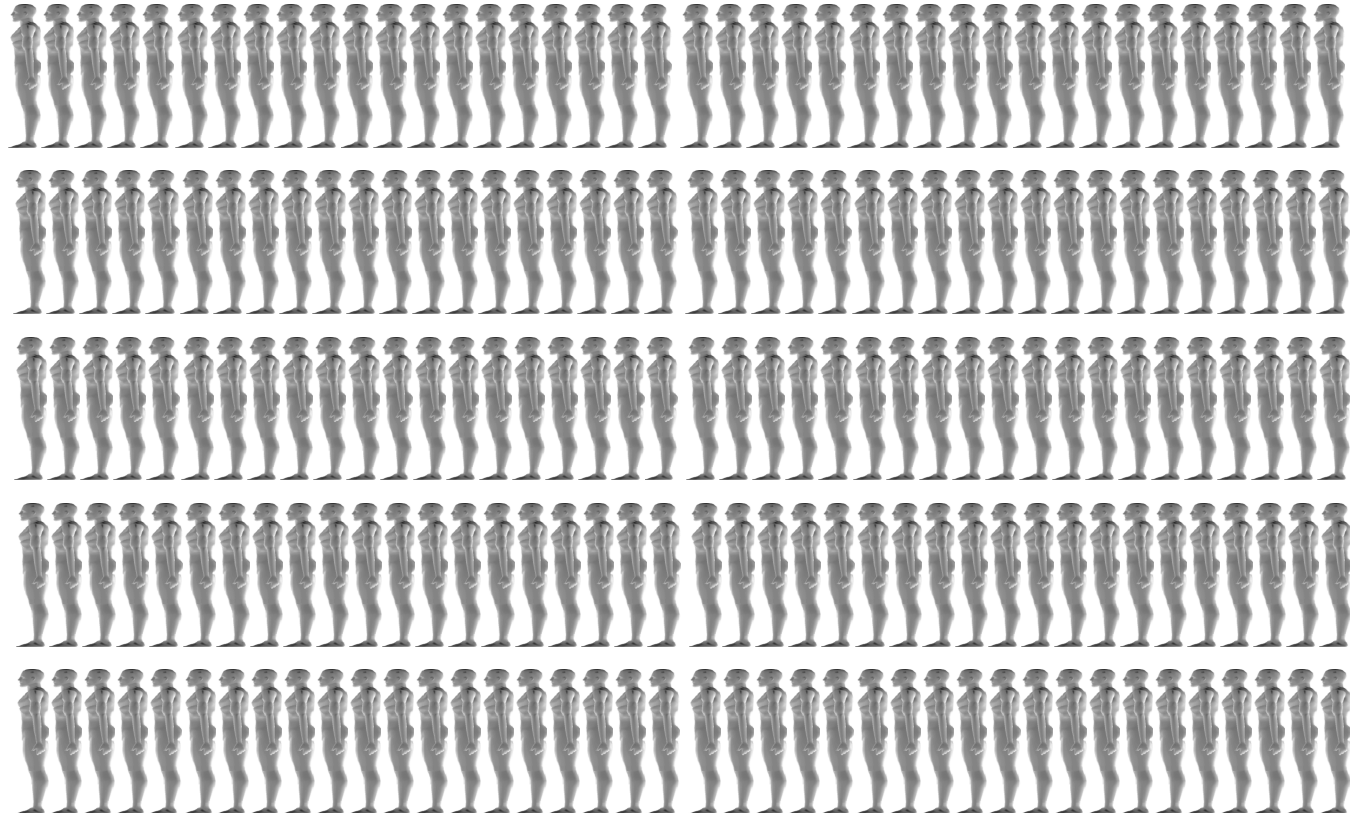
10ps TOFPET

Image More Often

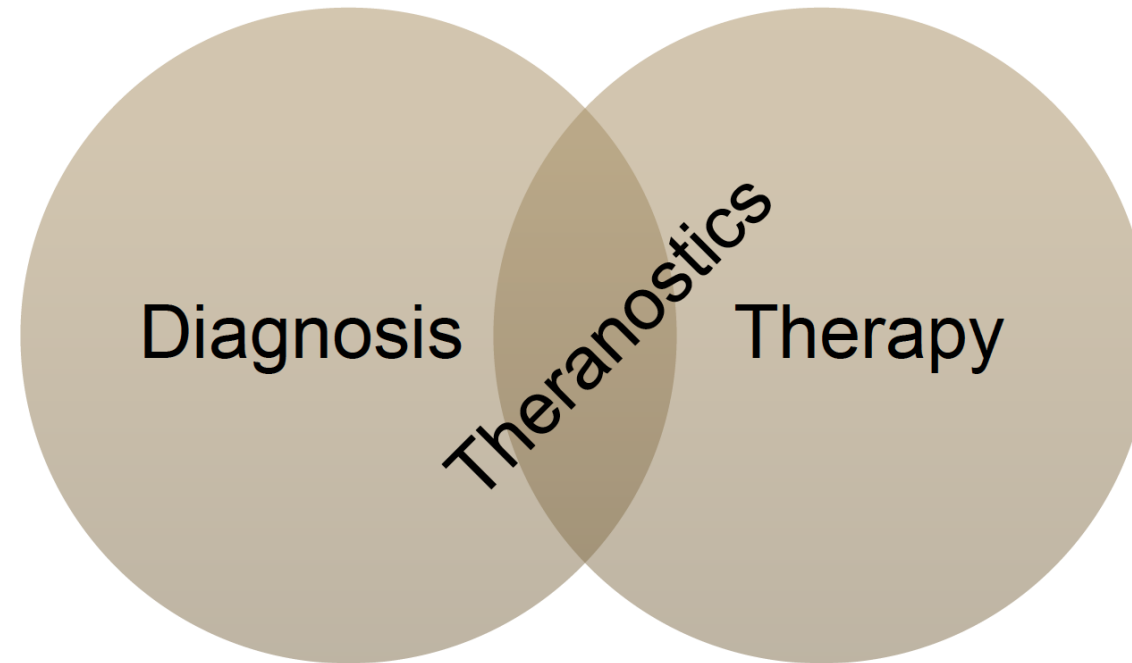
Conventional PET



10ps TOFPET



Radiopharmaceutical applications

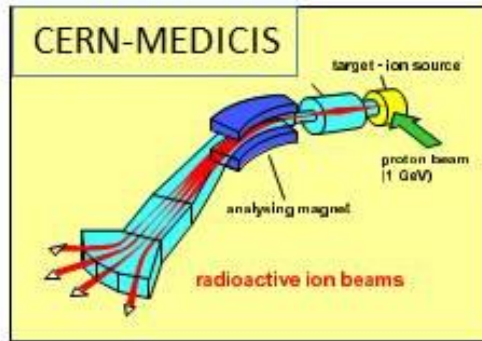


^{68}Ga -PSMA + ^{111}In -PSMA for diagnosis and therapy of prostate cancer

^{68}Ga -DOTATATE and ^{177}Lu -DOTATATE for diagnosis and treatment of neuroendocrine tumours

MEDICIS-PROMED: Innovative treatments based on radioactive ion beam production, transport and preclinical studies

Pure innovative
Radioisotope beams
from 2015 on



Mass purification
at medical cyclotrons



New packaging



Radiopharmaceuticals
targeting ovarian
cancer



Transport



Functional
Imaging



Theranostics
Isotope
Pairs

11C PET aided
hadrontherapy

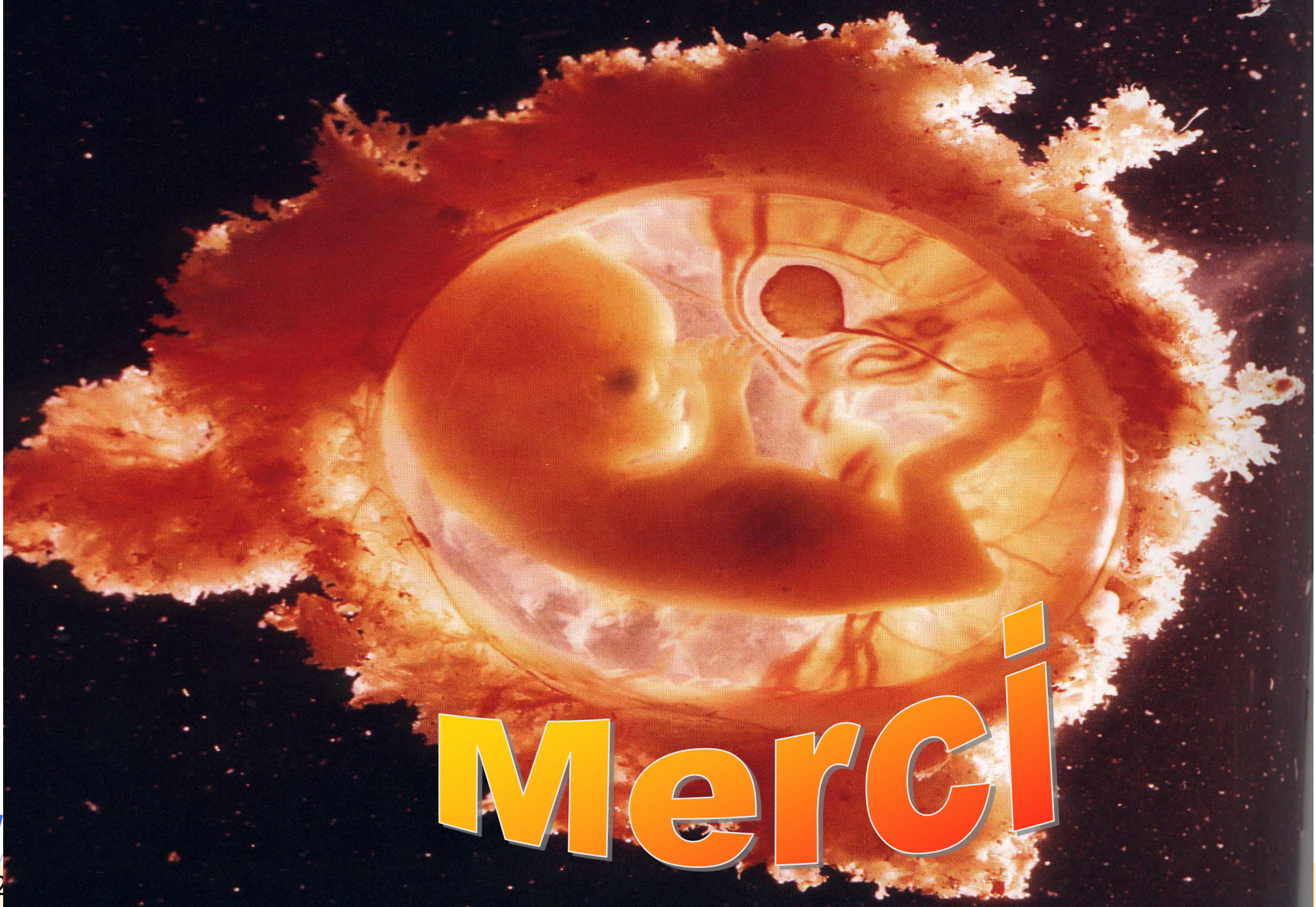
Tb 149	Tb 152	Tb 155	Tb 161
4.2 m	4.1 h	5.32 d	6.90 d
α	β^+	γ	β^-
α 3.99	β^+ 1.8	γ 87	β^- 0.5; 0.6...
γ 794	γ 344	γ 105	γ 26; 48; 75...
149	152	155	161

α, β^+

β^+

Auger

β^-



Merçi