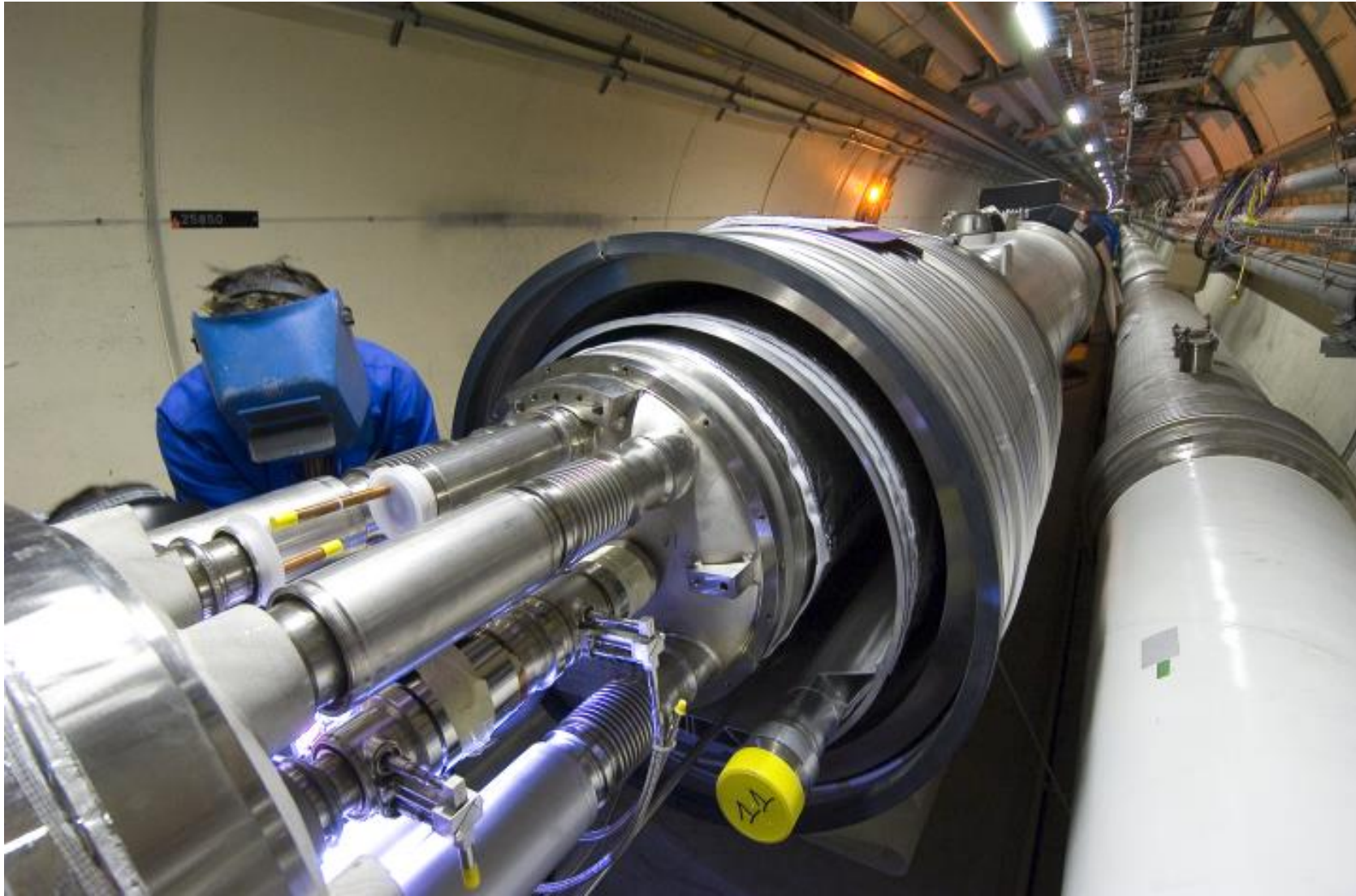




Physique et Imagerie Médicale

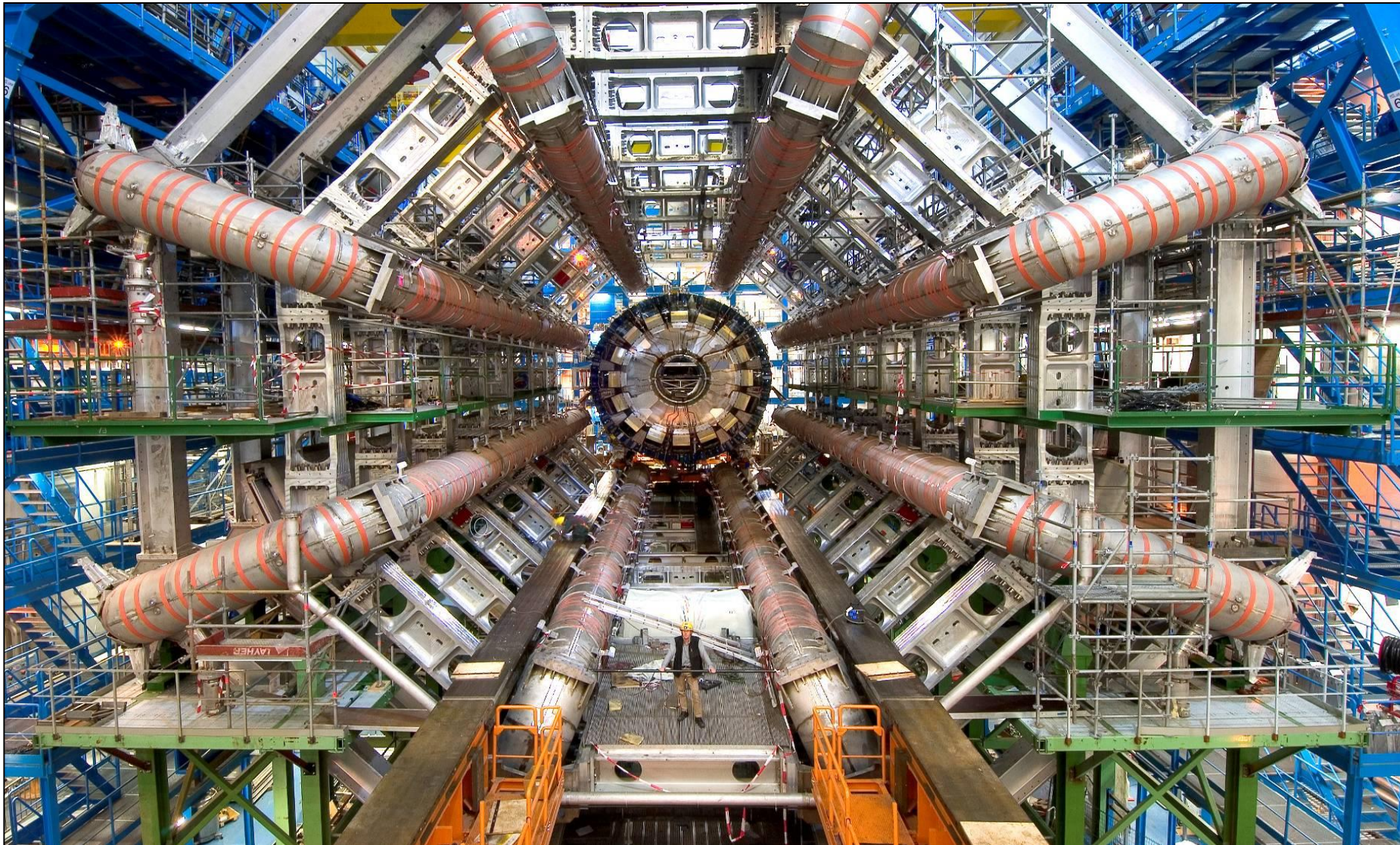
Paul Lecoq
CERN, Genève

LHC - Installation des aimants supraconducteurs (27km)

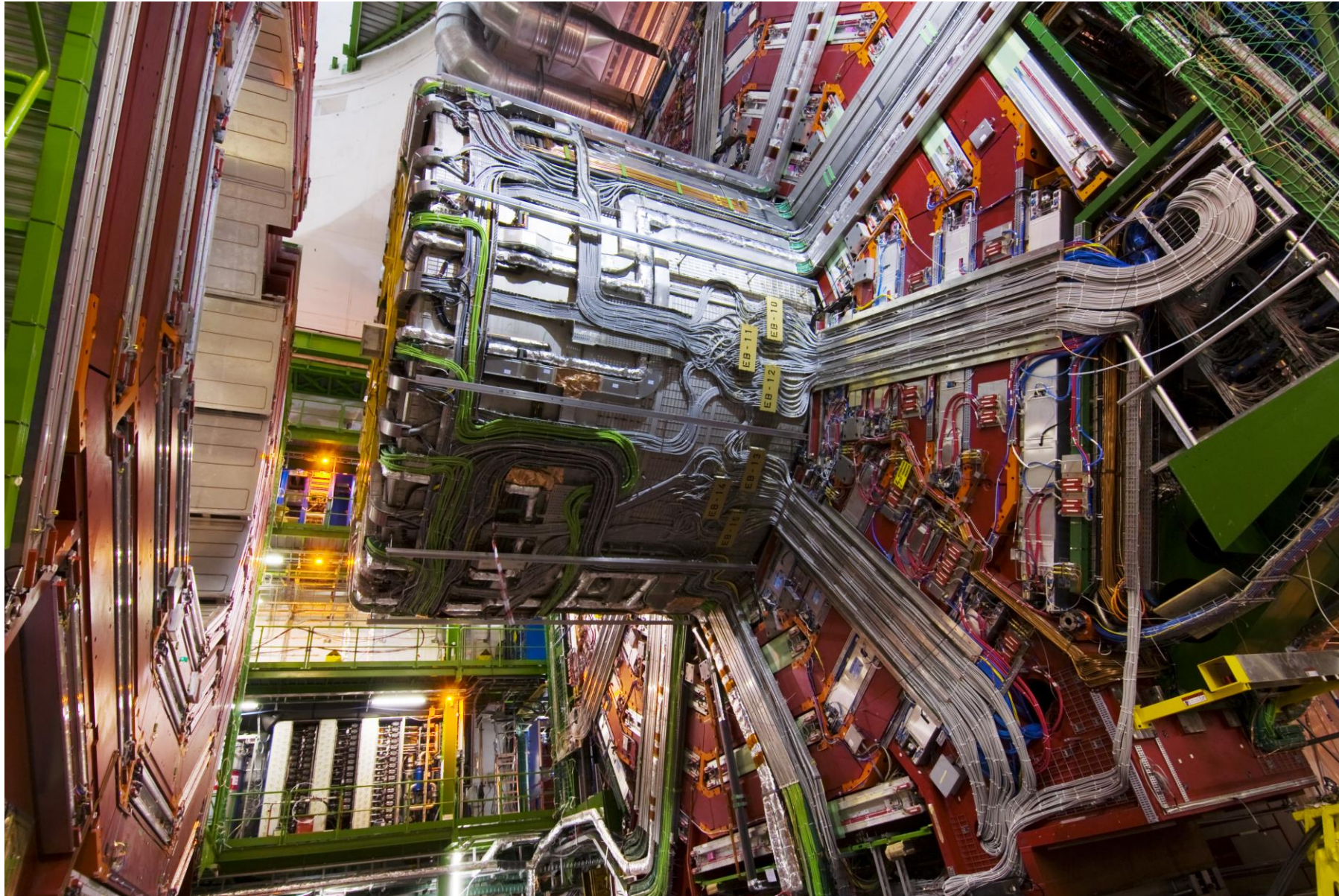




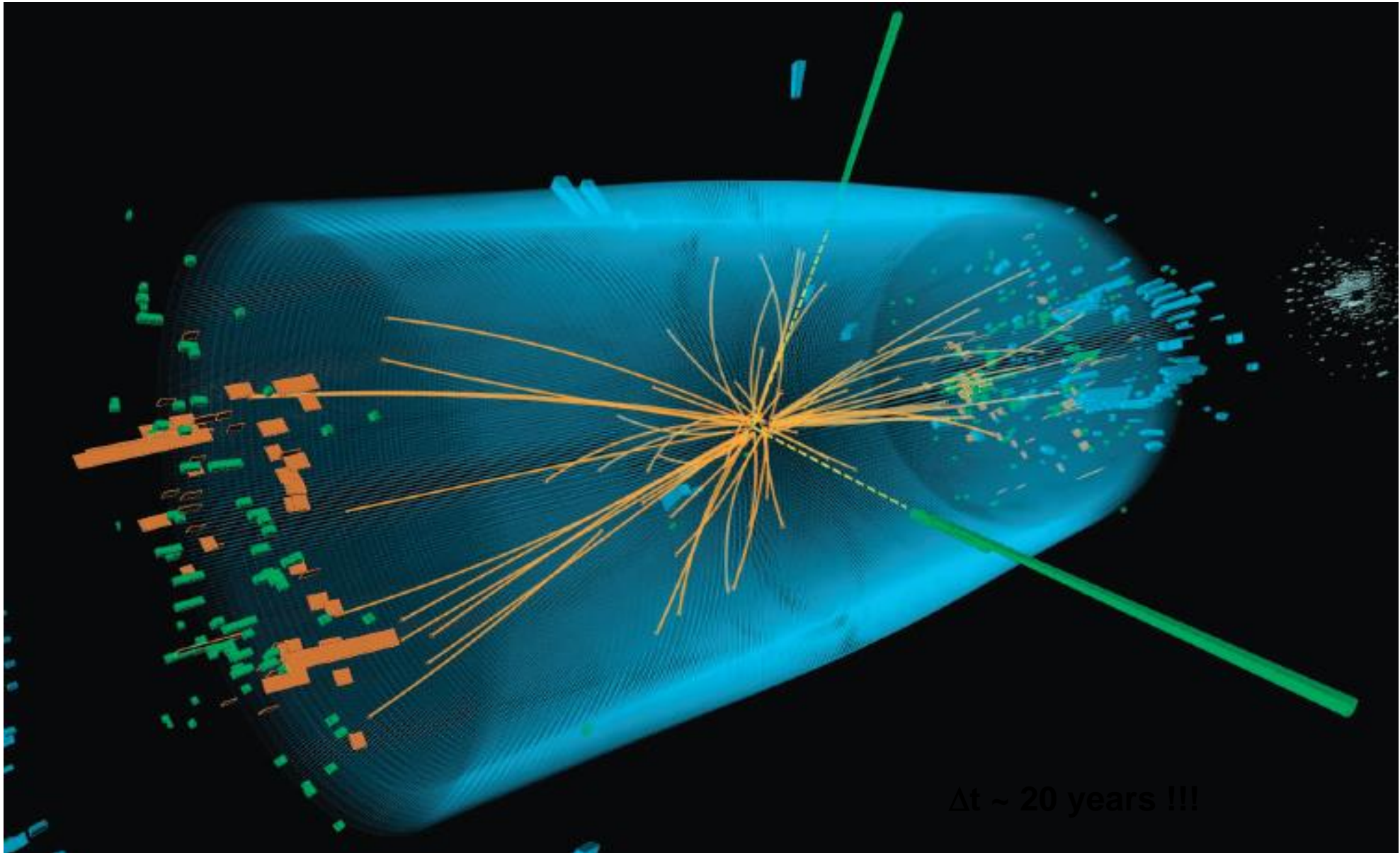
L'aimant toroidal d'Atlas



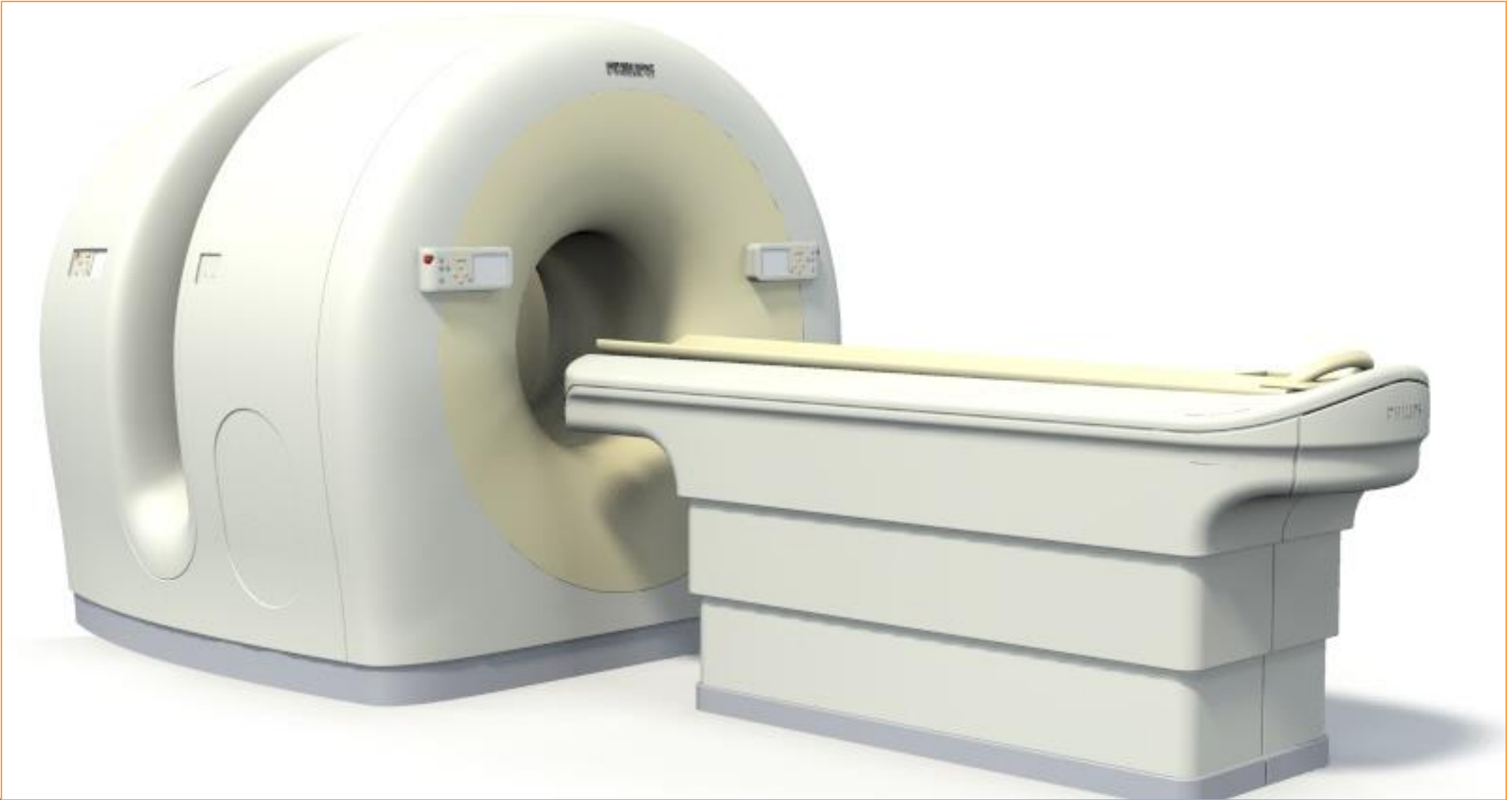
Montage de l'expérience CMS



July 4, 2012 : The Higgs Boson!!



Scanner TEP/CT





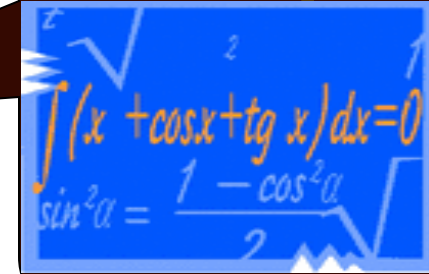
Patiente traitée
pour un cancer
du colon
révélant à
l'examen un
cancer du sein
additionnel

L'imagerie médicale: une approche pluridisciplinaire

Physique



Mathématiques



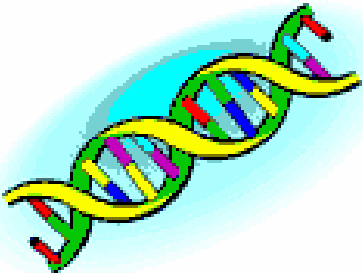
Médecine



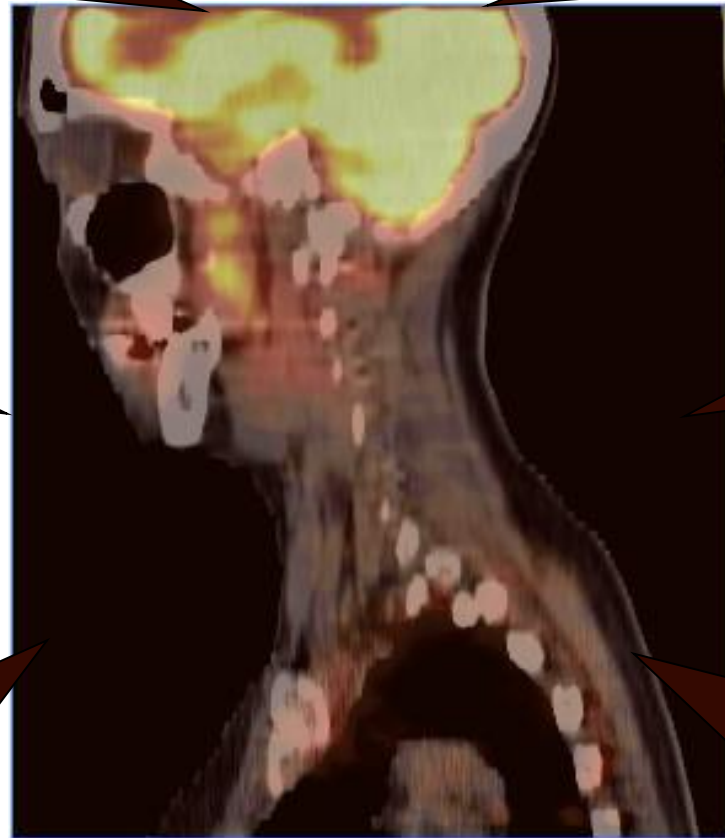
Chimie



Biologie




Informatique



La découverte des Rayons-X

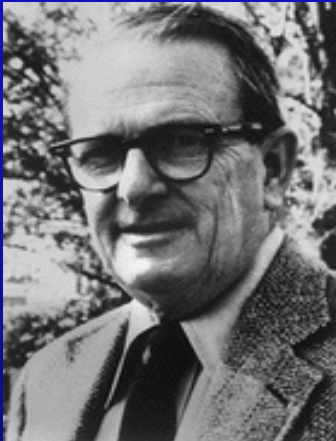
500'000'000
d'examens RX
chaque année dans le monde

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

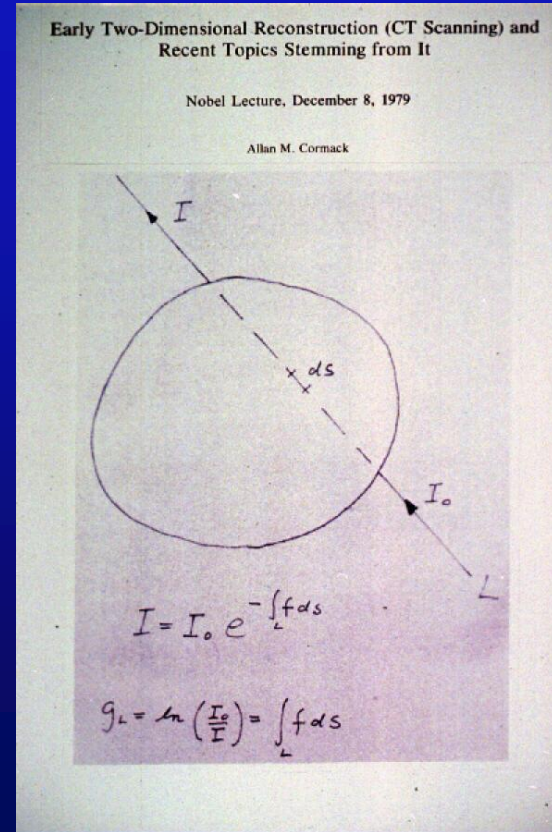


Röntgen obtient le 1^{er} prix Nobel de physique en 1901

Prix Nobel de Physiologie et Médecine 1979

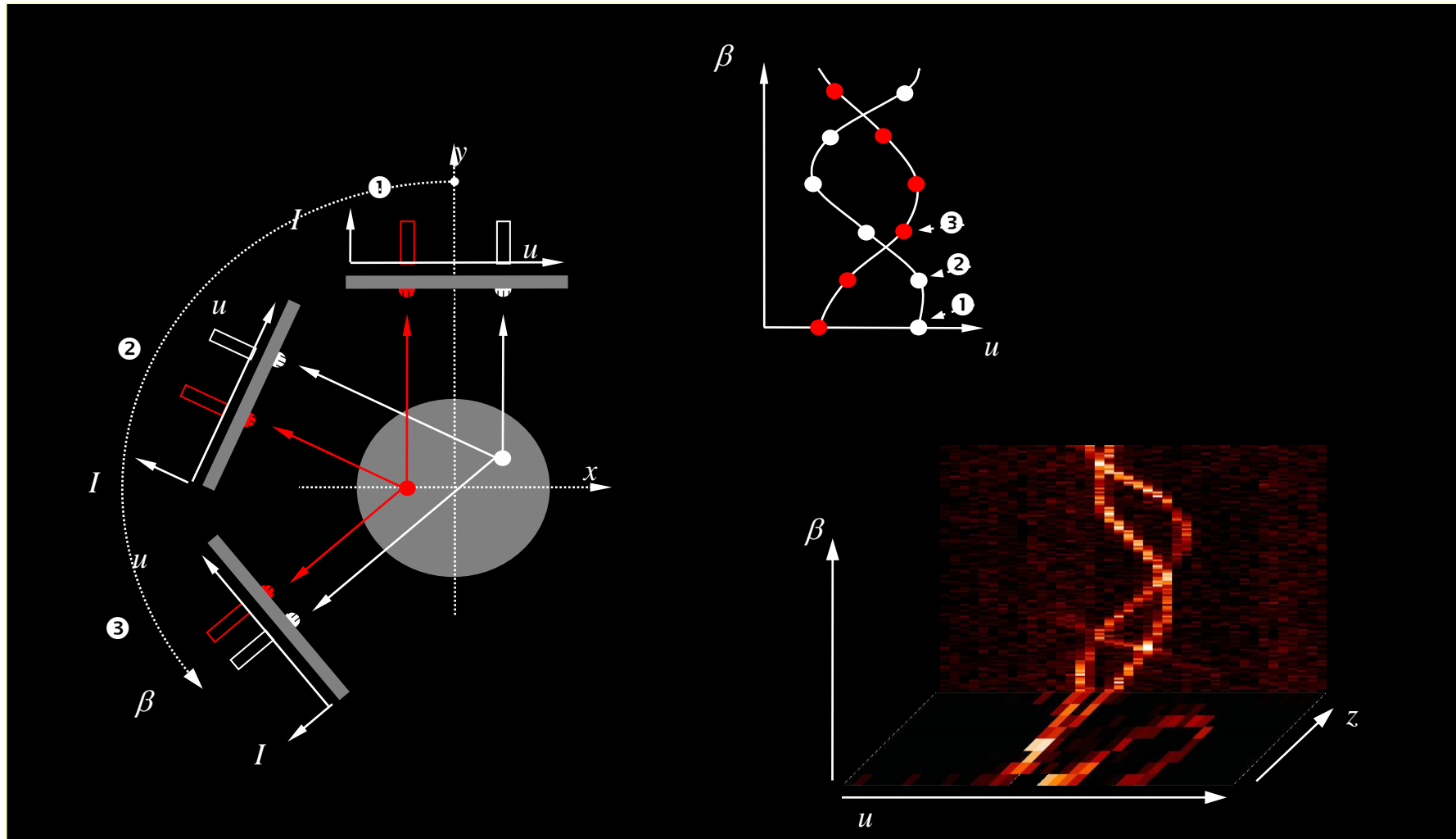


Allan MacLeod Cormack
Physicien Nucléaire
Cape Town
Harvard University
Tufts University

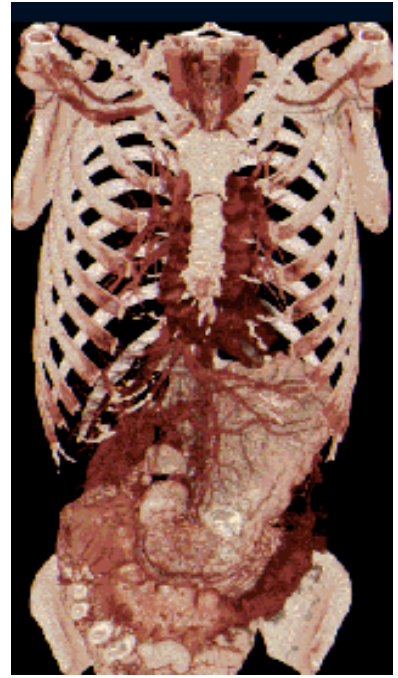
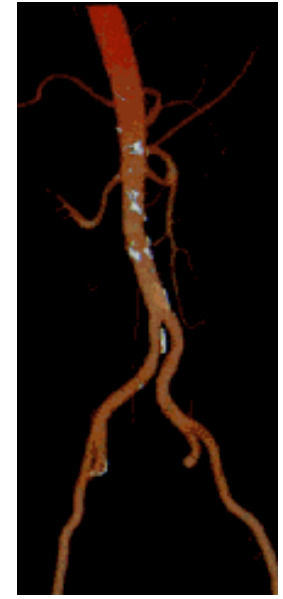
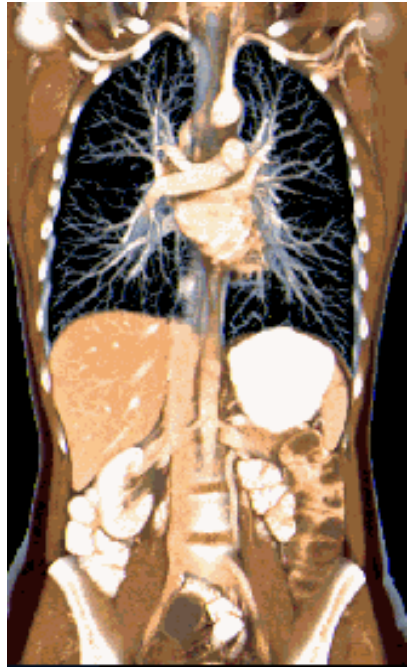


Sir Godfrey N. Hounsfield
Ingénieur électricien anglais
EMI Research

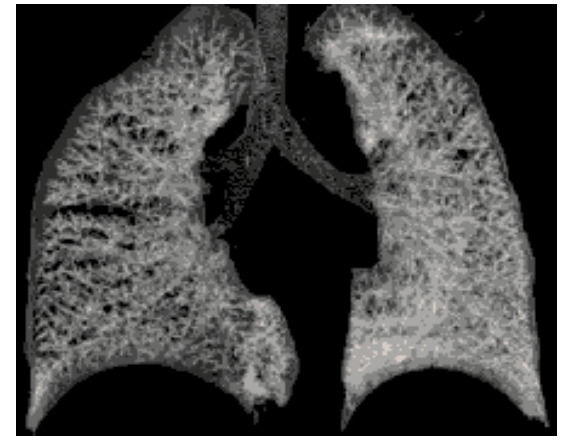
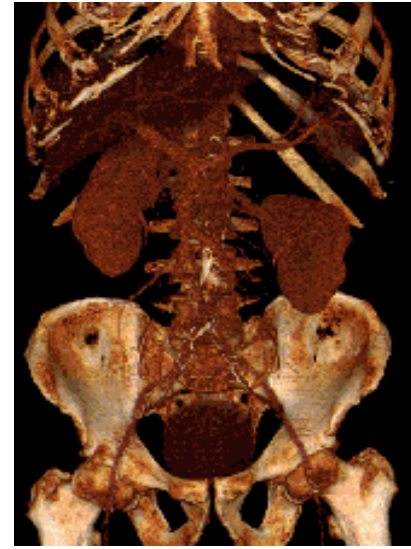
Principe de la Tomographie

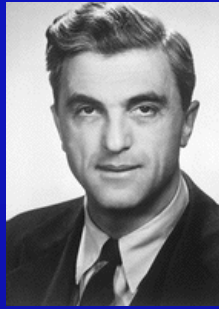


Tomographie volumétrique



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





Felix Bloch
Physicien Stanford

Prix Nobel de Physique 1952

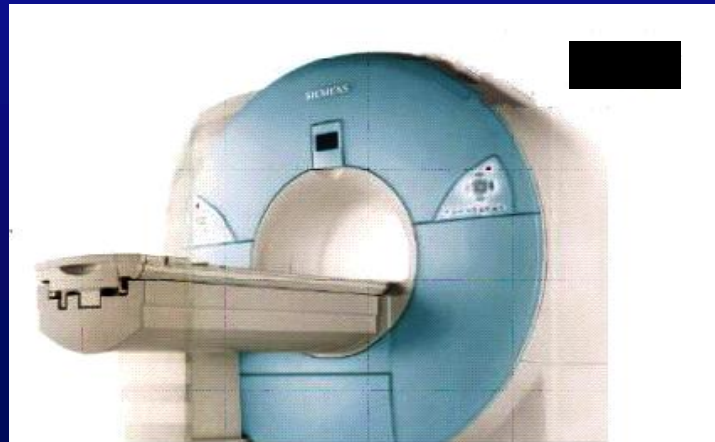


Edward M. Purcell
Physicien Harvard

Prix Nobel de Physiologie et Médecine 2003

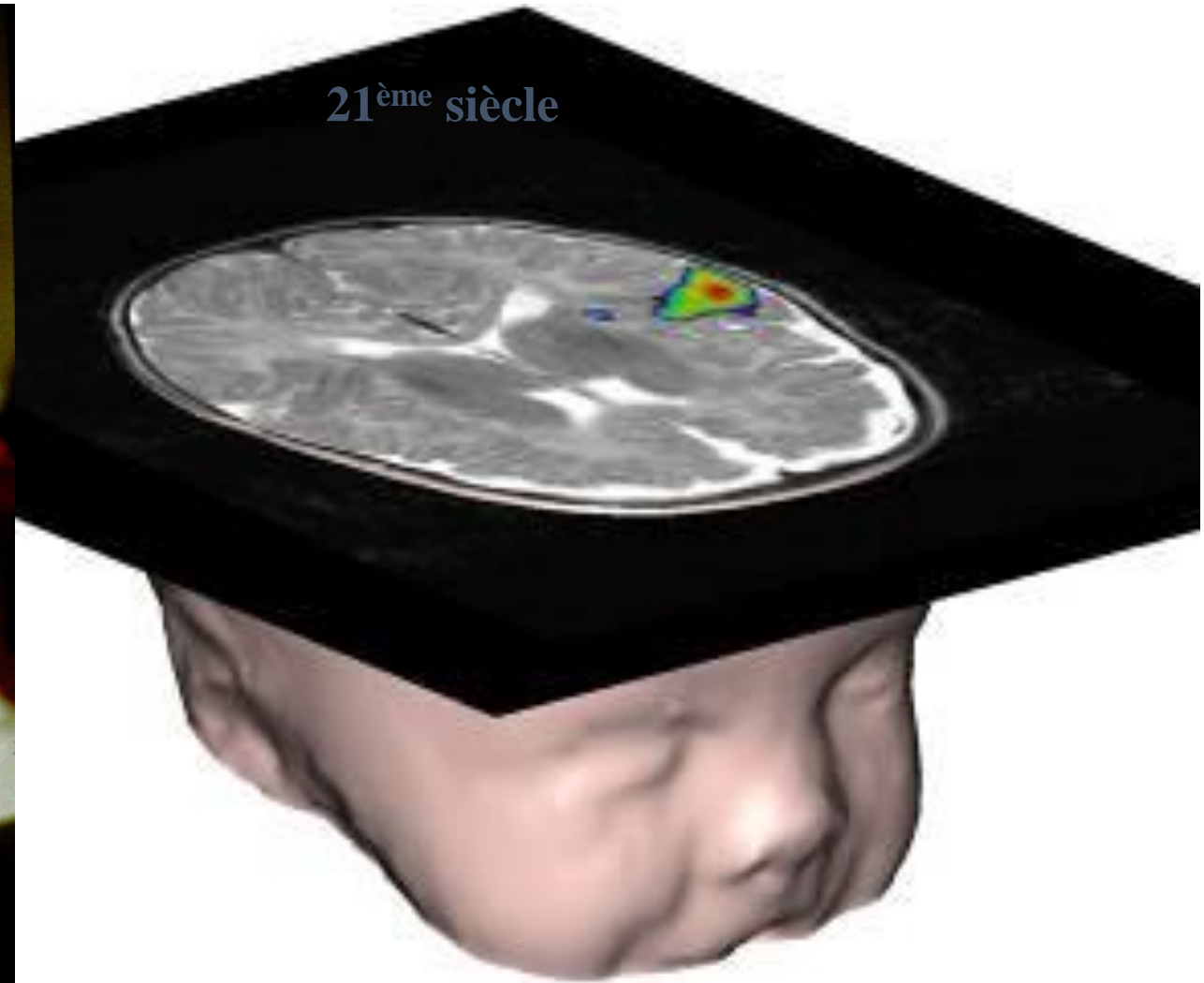


Sir Peter Mansfield
Physicien Nottingham



Paul C. Lauterbur
Chimiste Uni. Illinois

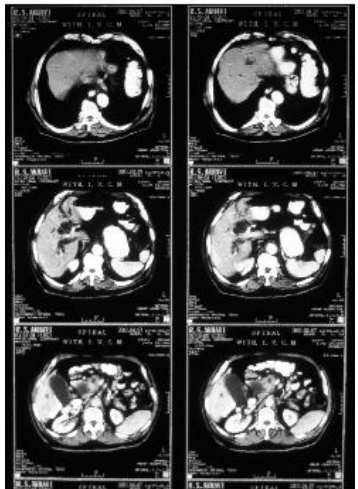
Petite histoire résumée de l'imagerie in-vivo



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 des 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)*

Imaging Modalities



CT

A Tissue Density, Z
20-50 μm

Ultrasound



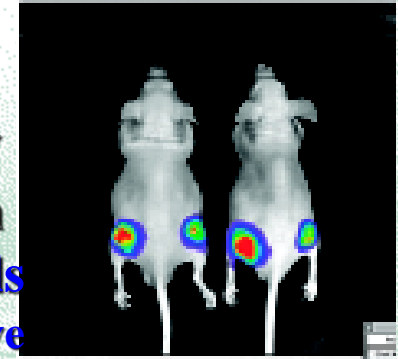
A **F**

Structure
0.1 mm
Doppler

Optical (Bioluminescence, fluorescence)

A **M**

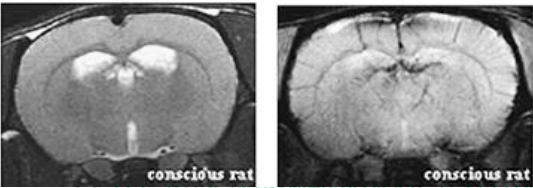
Topography
 μm to mm
 $\sim 10^3$ cells
 \neq quantitative



Photons involved

4.7T, Dual Coil, Coil, T1 Weighted SE

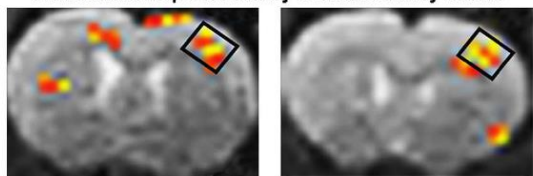
4.7T, Dual Coil, T2 Weighted GE



conscious rat

conscious rat

Activational Maps of Primary Somatosensory Cortex



MRI

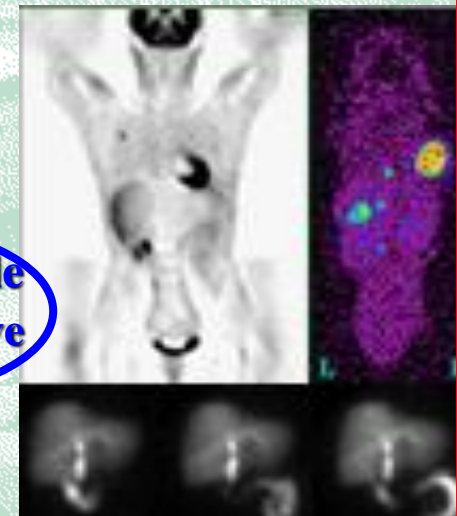
A **F** **M**

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

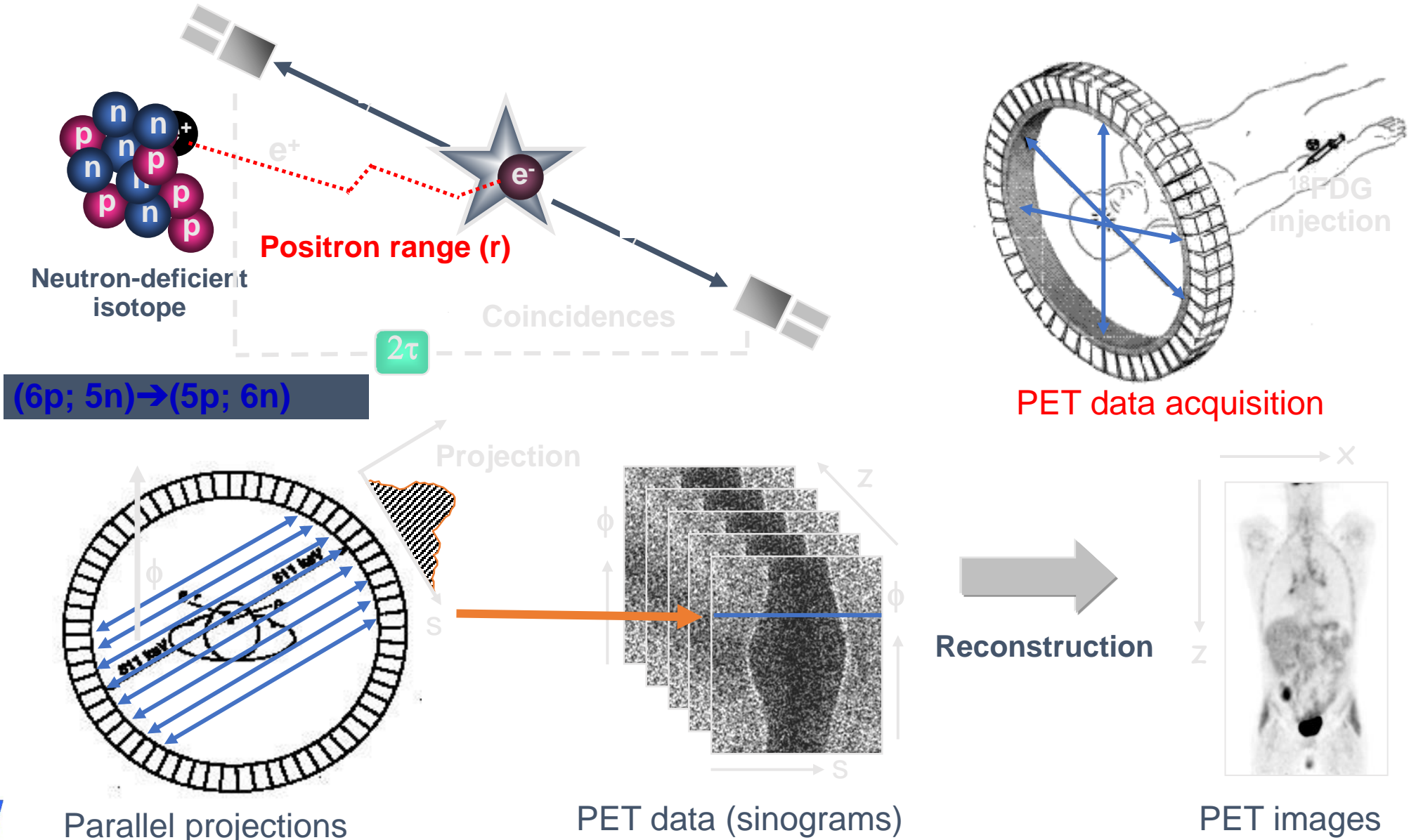
PET/SPECT

F **M**

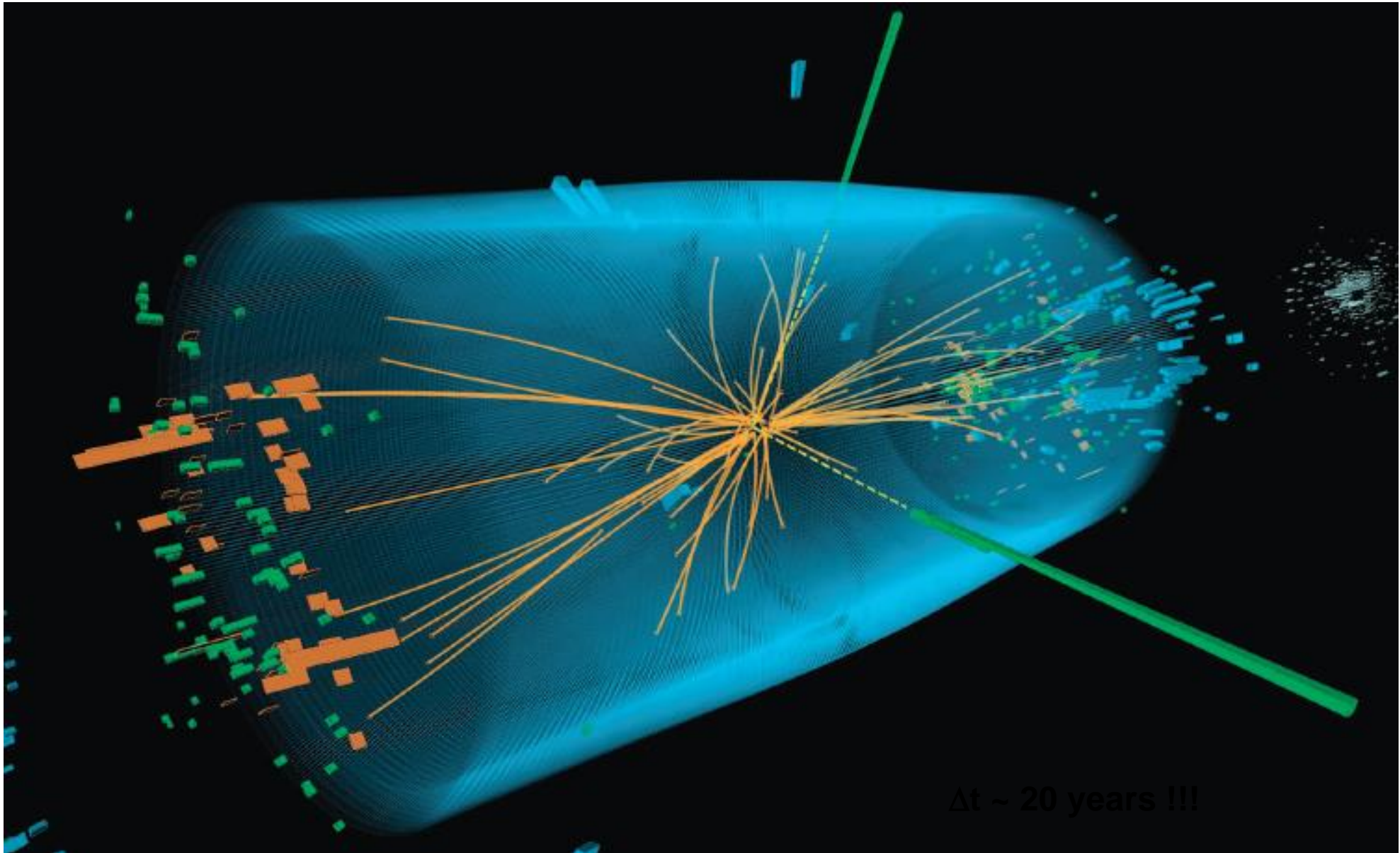
Radiotracer
 $\sim 1\text{-}2$ mm
 $< 10^{-12}$ mole
 $=$ quantitative



PET Principle



July 4, 2012 : The Higgs Boson!!



The PET World Picture

Need to Image
0.000000511 TeV*
Photons

*511 keV

Signal Levels Are Very Low

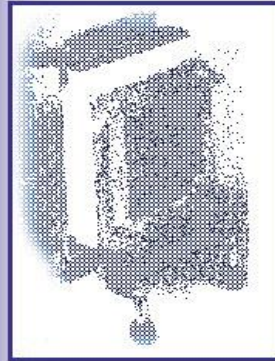
1977

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



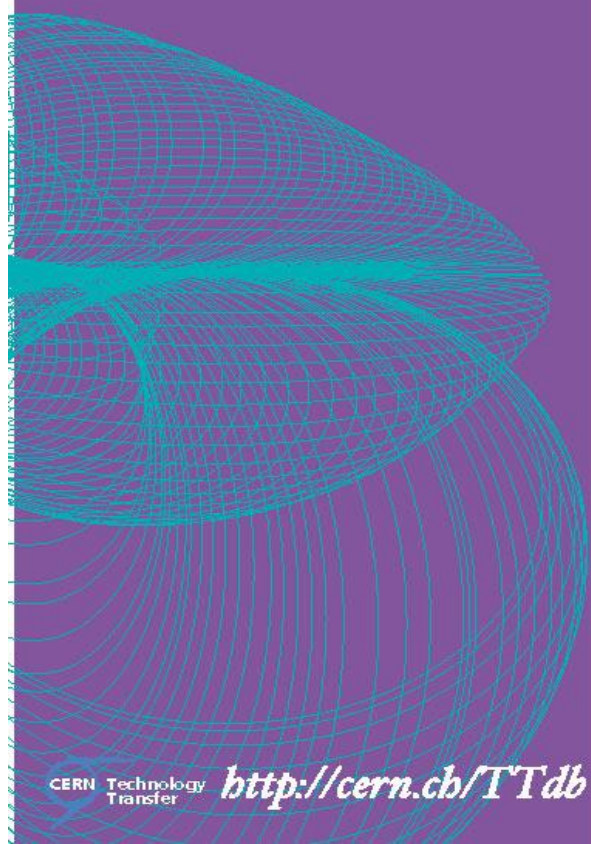
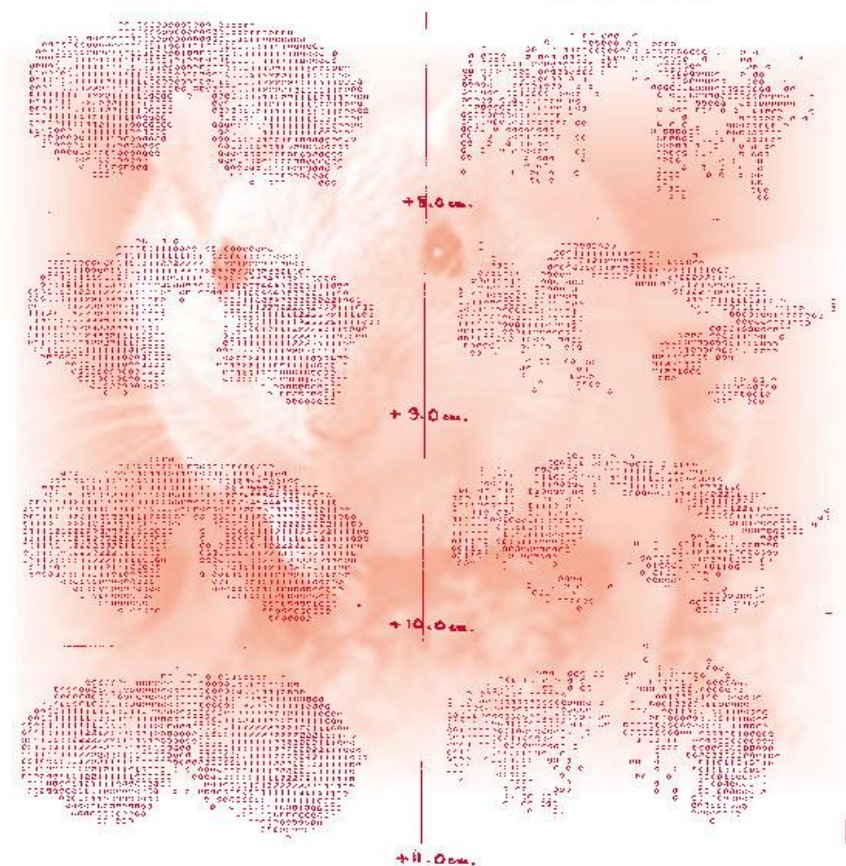
(Jeavons, Townsend et al)

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

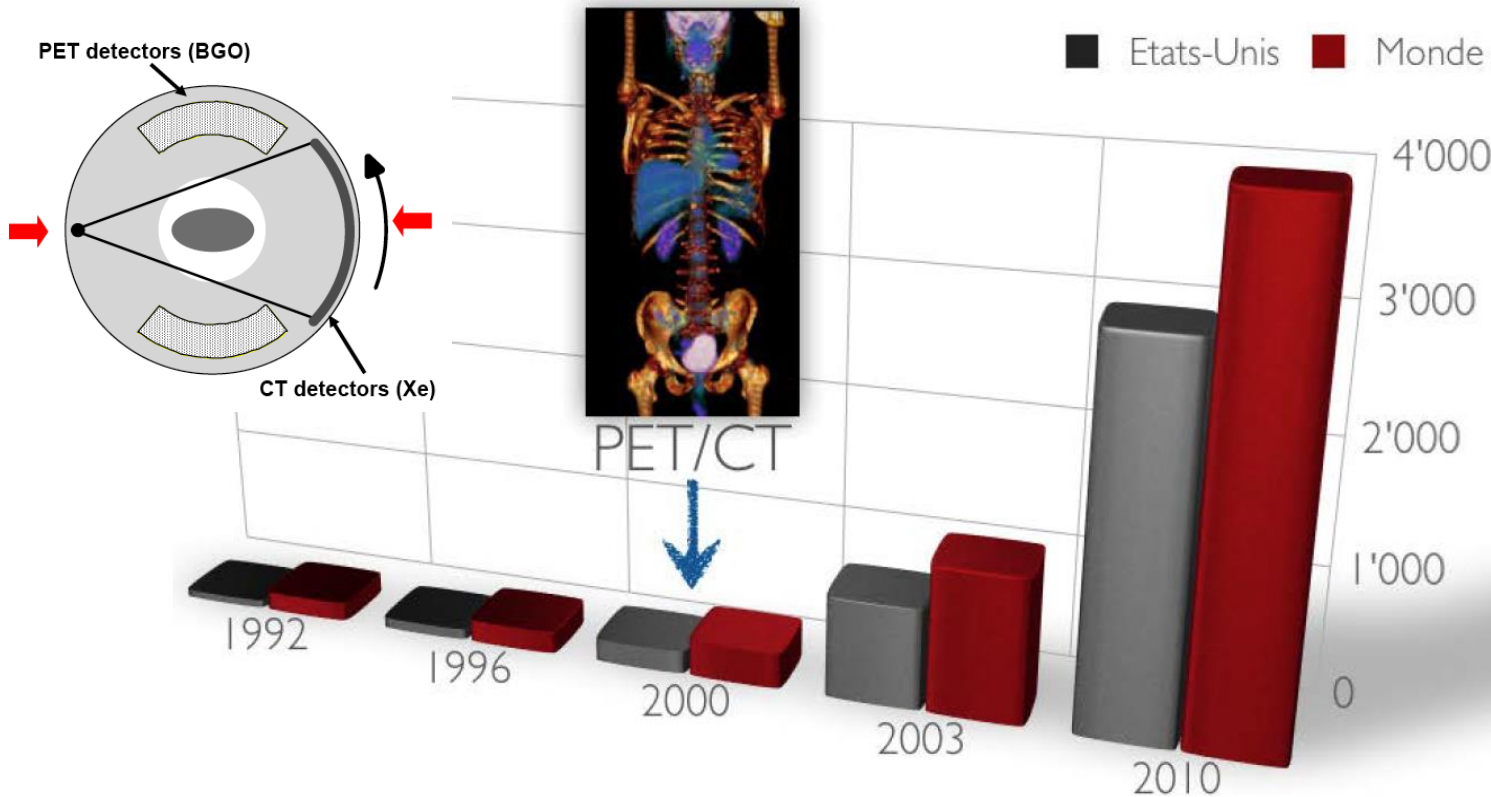
PET/CT



TIME
DECEMBER 4, 2000

Time Magazine's
Medical Invention
of the Year 2000

Disruptive Technology



PET/CT Invention

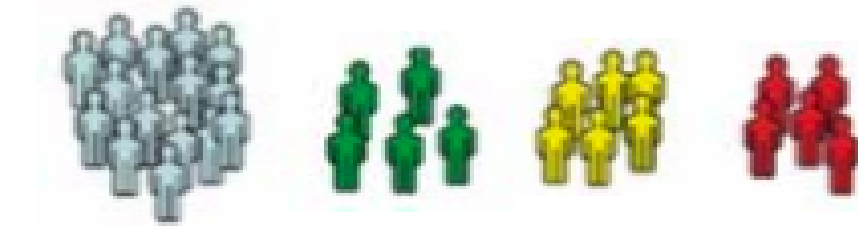


David Townsend
(former CERN)

Médecine personnalisée

Approche globale

Médecine personnalisée



Un diagnostic



Un traitement



Diagnostic moléculaire



Imagerie moléculaire

+ Génomique



Traitement individualisé

L'imagerie pour une meilleure prise en charge du patient

Recueillir une information détaillée de chaque individu pour:



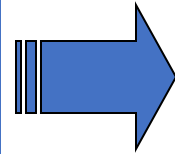
- Diagnostiquer la maladie à un stade précoce
- Déterminer les paramètres de la maladie, comme son agressivité, son potentiel métastatique
- Optimiser l'action thérapeutique en fonction du génotype du patient
- Evaluer instantanément l'efficacité du traitement

*Implique une nouvelle génération
de systèmes d'imagerie*

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

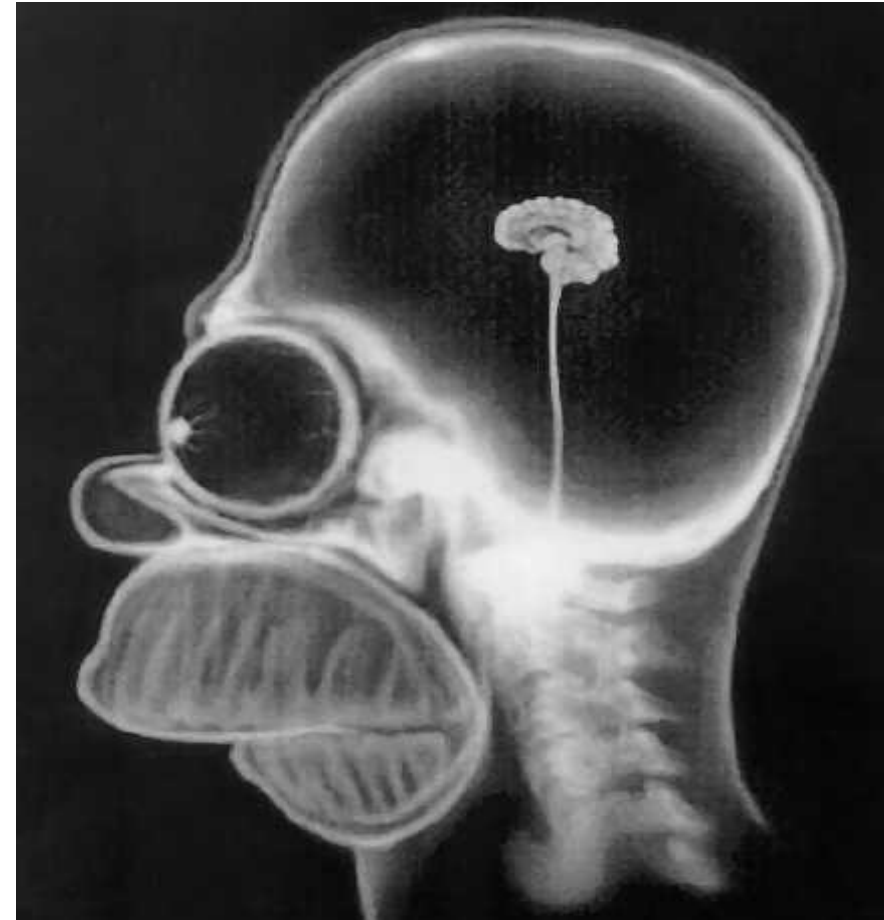
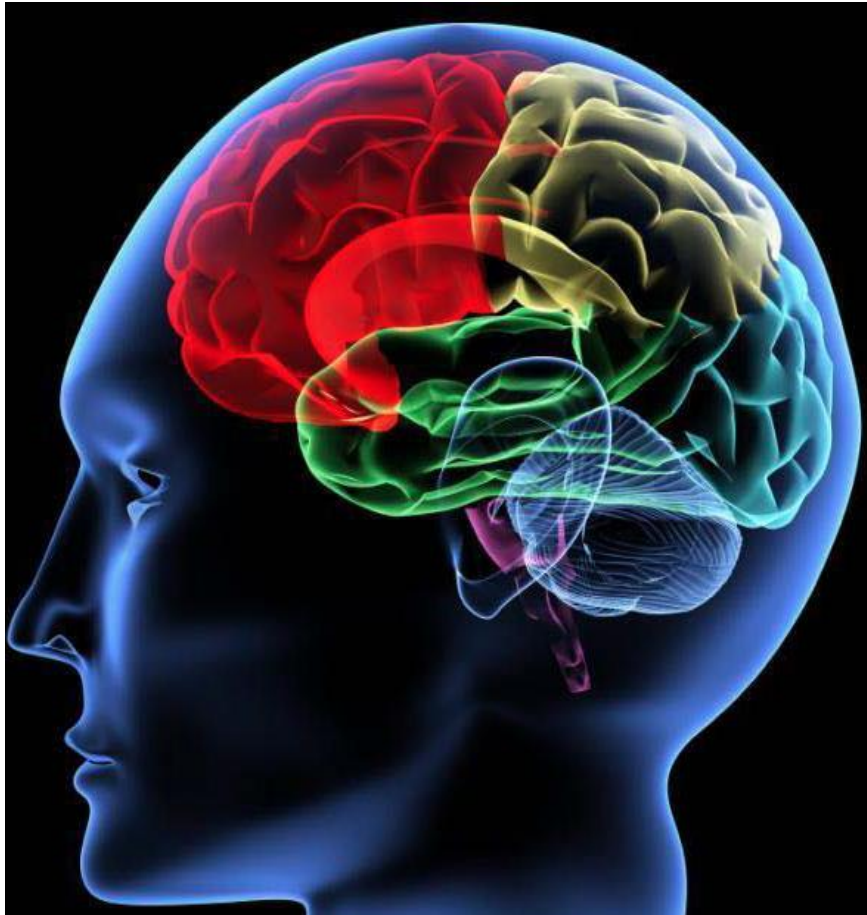
Etudes de plus en plus spécifiques sur modèles animaux

- 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 2x2x5mm³ lus par des matrices de 4x8 APD et 0.18µm CMOS ASIC

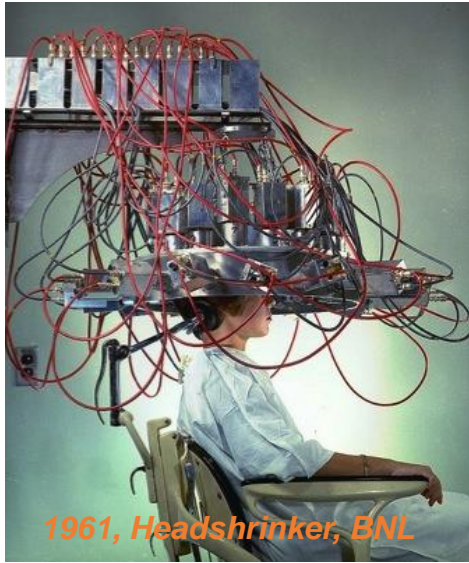
•C. Woody et al. Several papers in conference records of NSS/MIC2004, Rome



Courtesy of C. Woody, BNL



Brain Imaging



1961, Headshrinker, BNL



2011, PETHAT, Hamamatsu



2013, BrainPET, Hamamatsu



2008, RATCAP, BNL



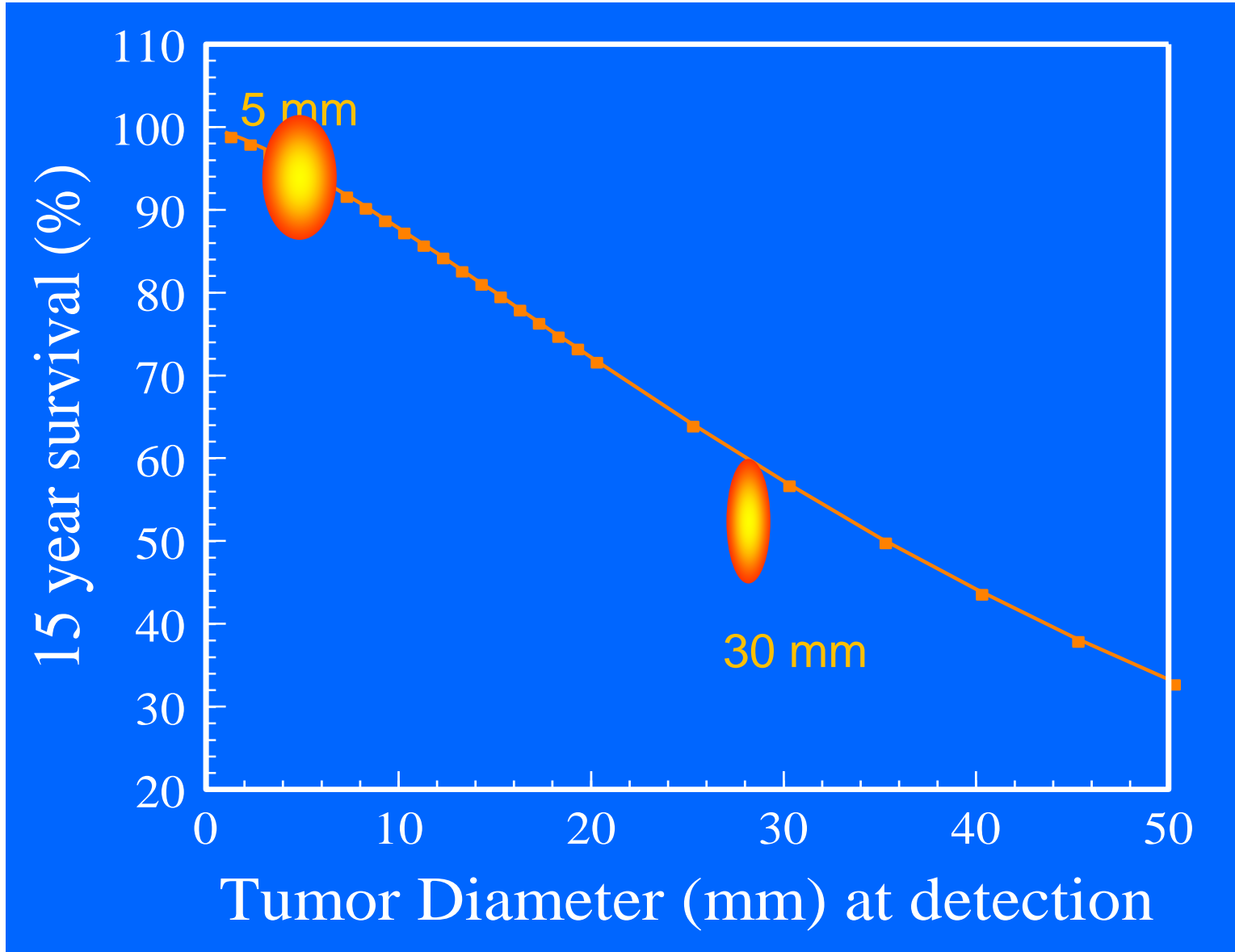
2012, HELMETPET, Majewski



2015, HELMET CHIN, Yamaga

Courtesy: S. Majewski, West Virginia University

Breast Cancer

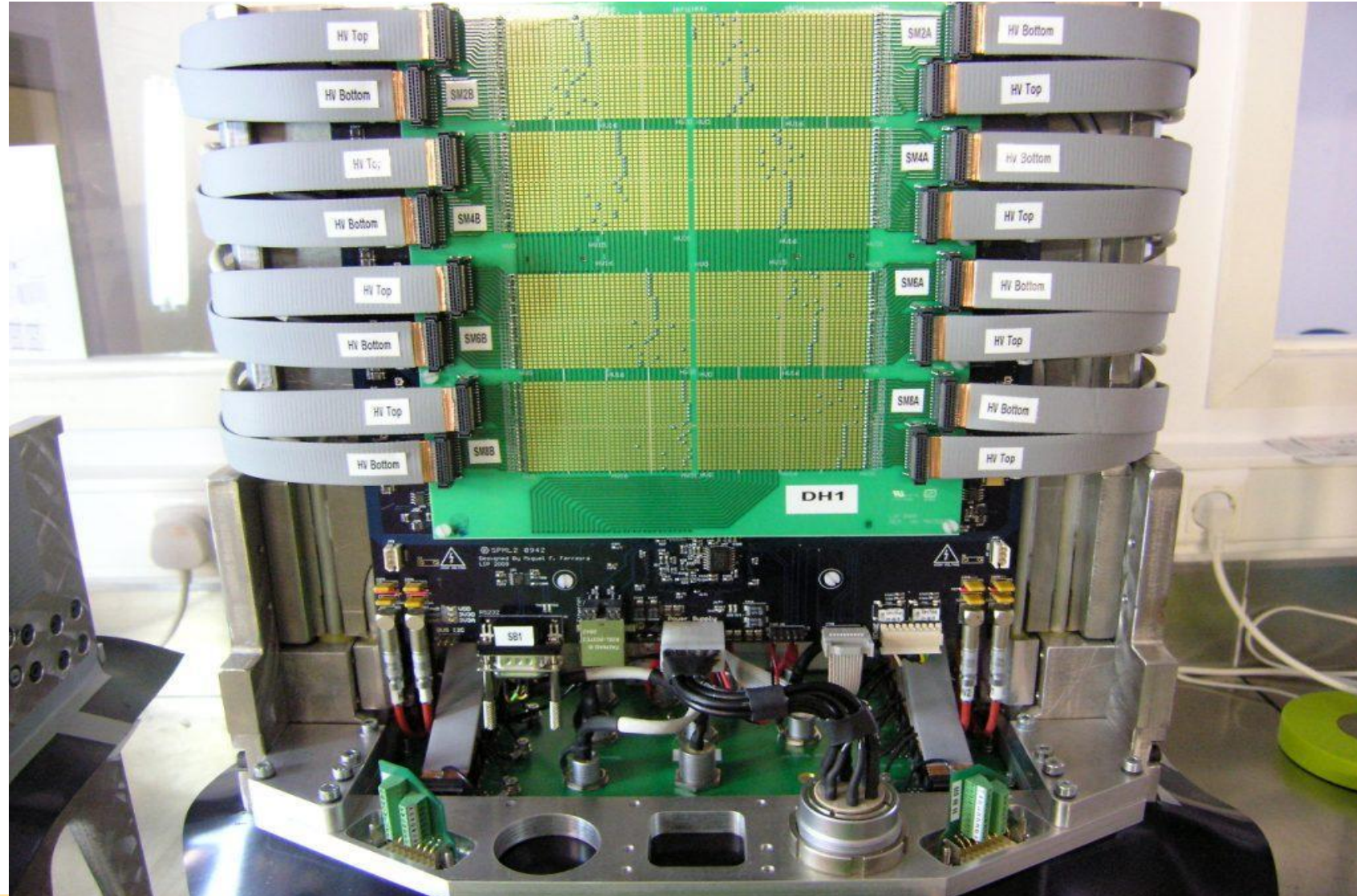


ClearPEM-Sonic a collaborative project between physicians and physicists



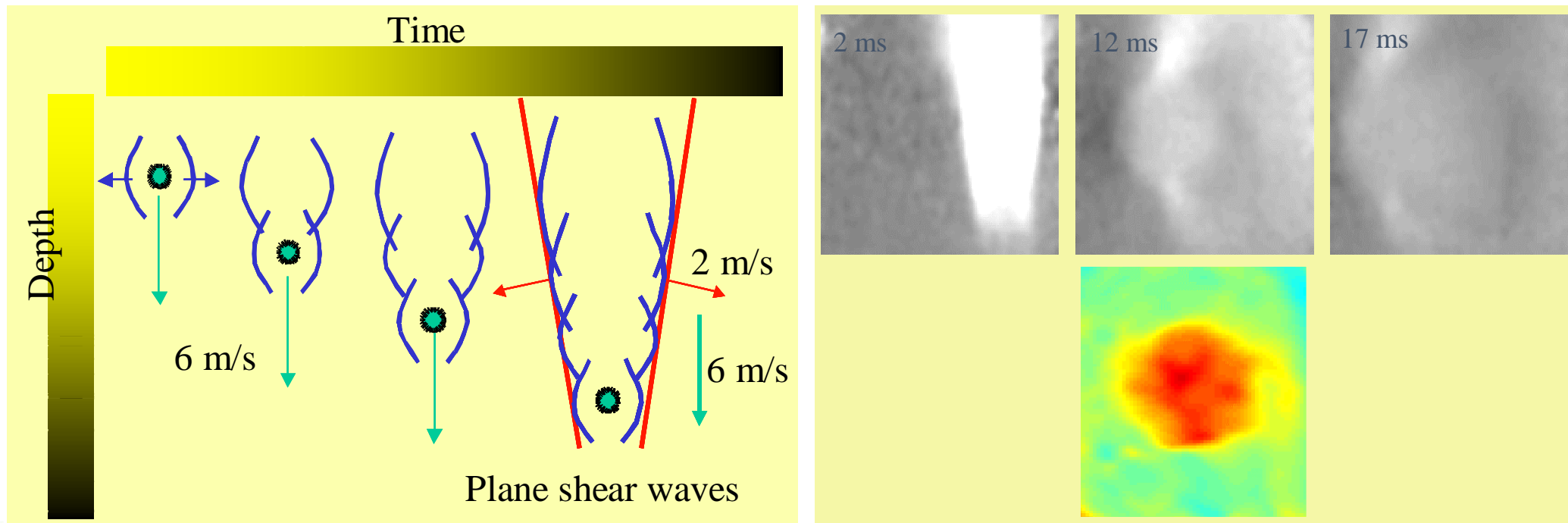
Objective: Detect 3mm tumors and define their cancerous status

Des technologies d'avant-garde: ClearPEM

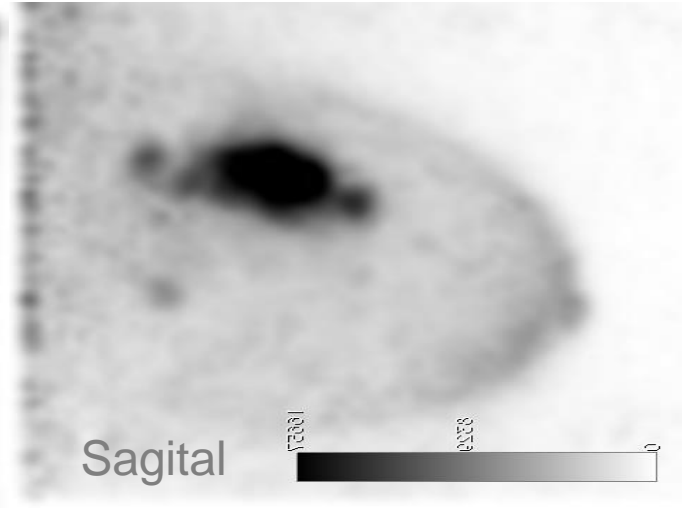
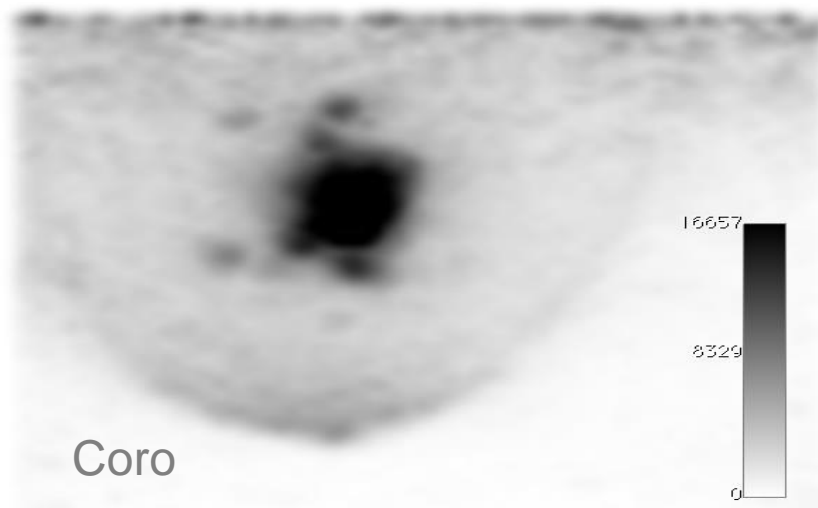
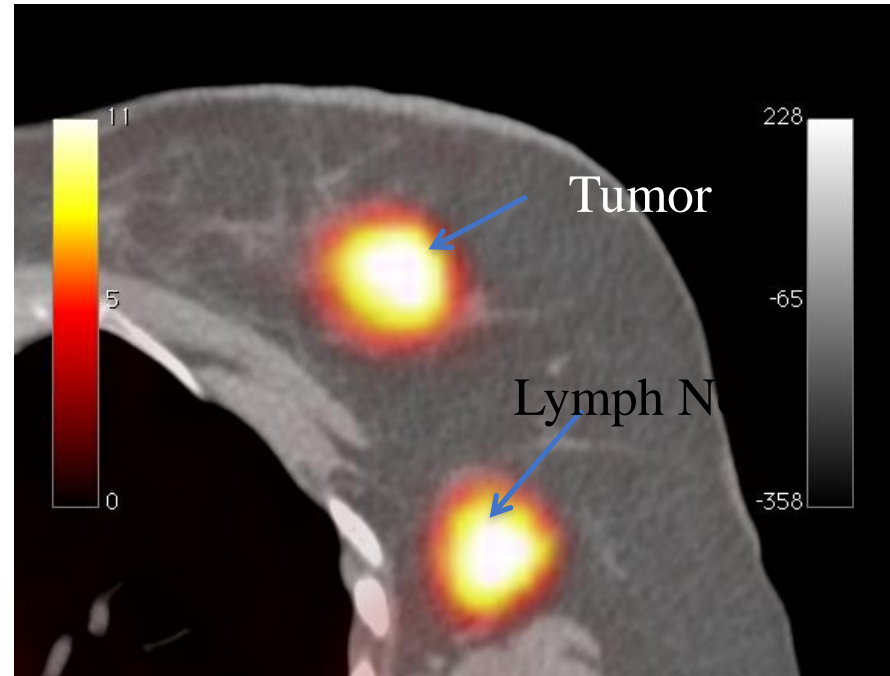


Des technologies d'avant-garde: Ultrasons

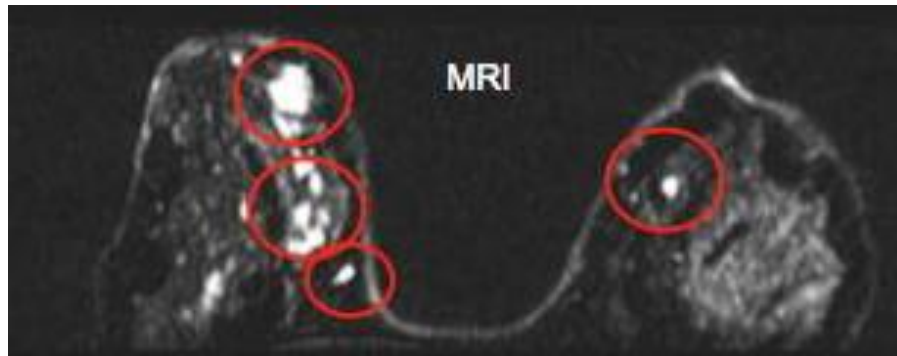
- Focus ultrasound beam in tissue
- Propagate focal point at a supersonic speed in breast
- Measure the deformation of the shock wave by a tumor



Benefit of dedicated breast PET imaging



PET/MRI complementarity



4 lesions identified on MR image



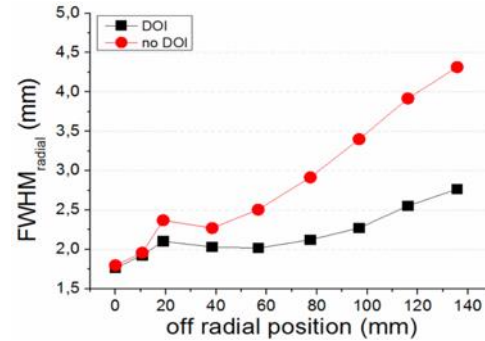
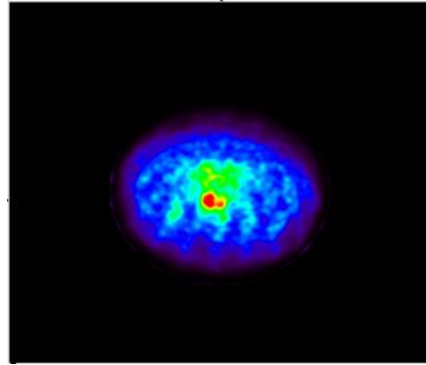
Only one suspicious lesion identified on PET image

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

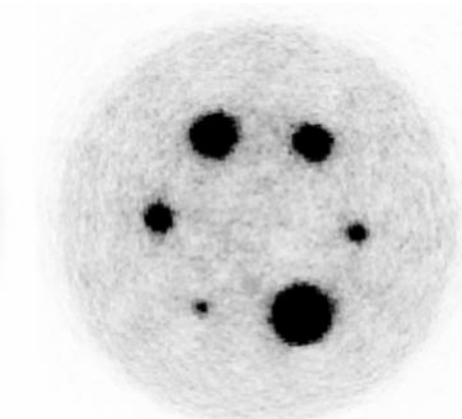
Courtesy: Dr. José Ferrer, ERESA, Hospital General Universitario de Valencia, Spain

Other organ specific PET

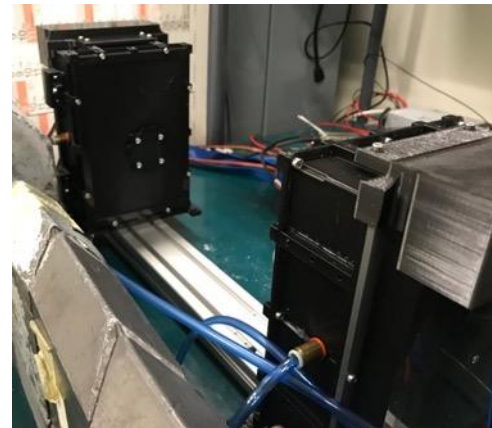
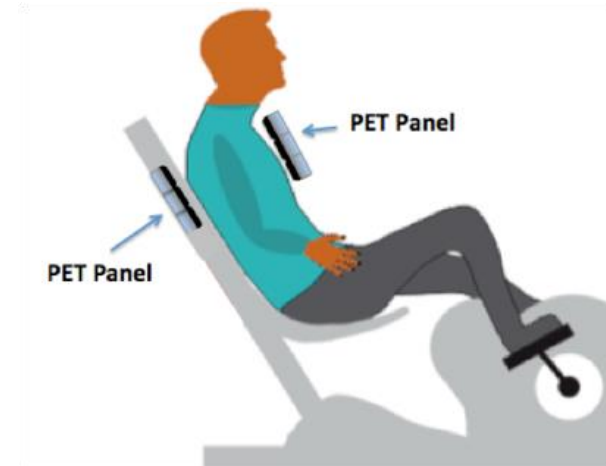
ProsPET



GeminiTF



ProsPET

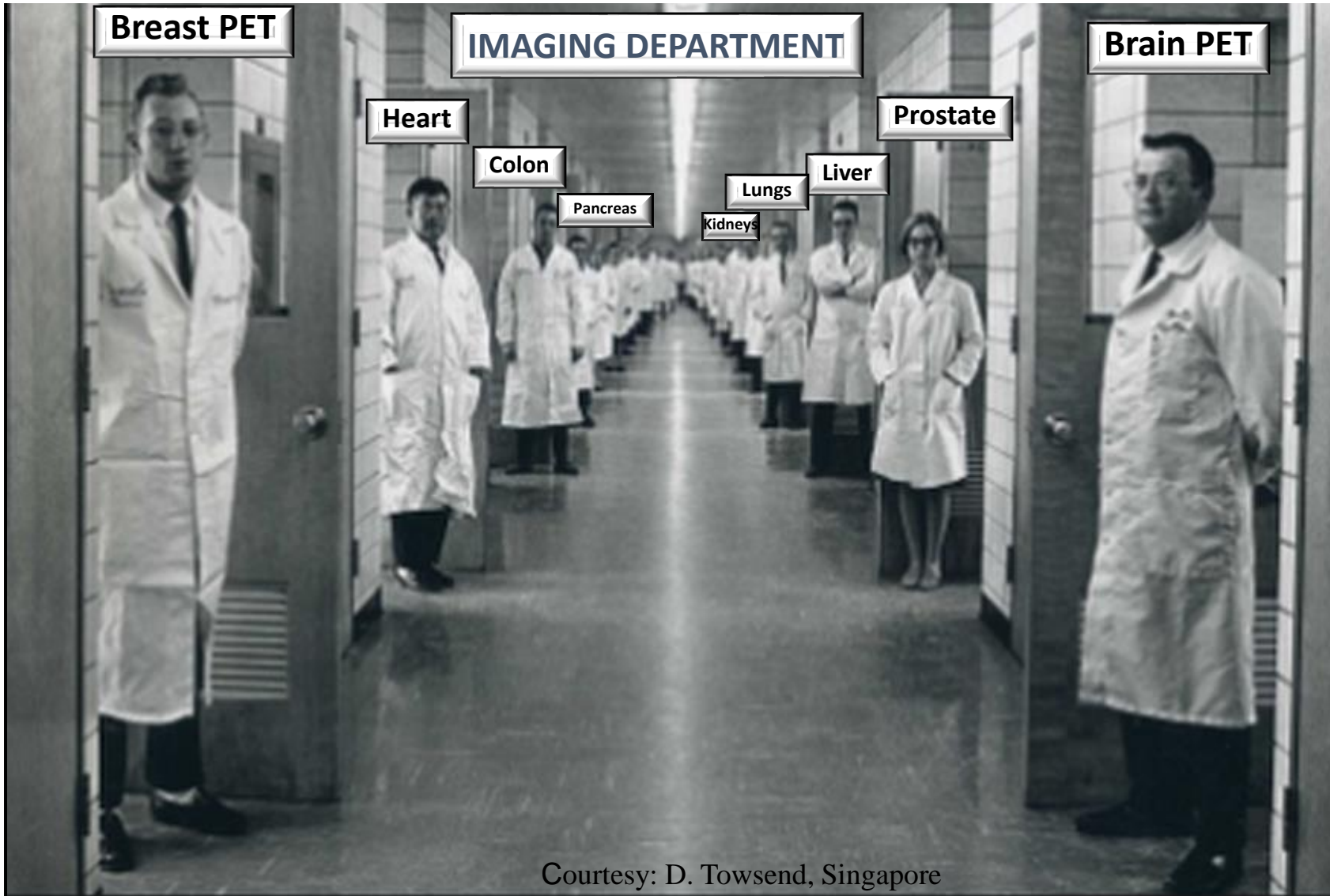


State-of-the-Art results

- Timing resolution < 250 ps
- Energy resolution near 11.5@511keV
- Spatial resolution 3 mm

CardioPET

Personalized medicine → Organ-specific imaging devices



Courtesy: D. Townsend, Singapore

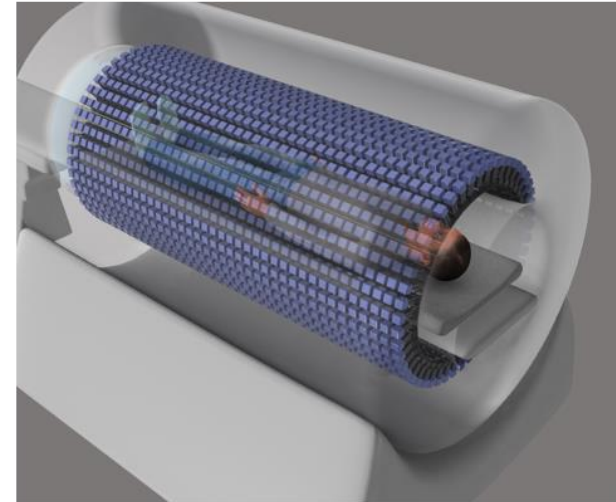
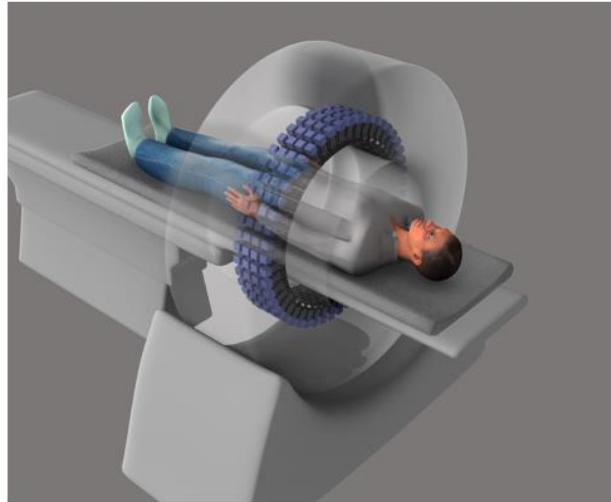
Increasing effective PET sensitivity

- 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)

Improve solid angle coverage

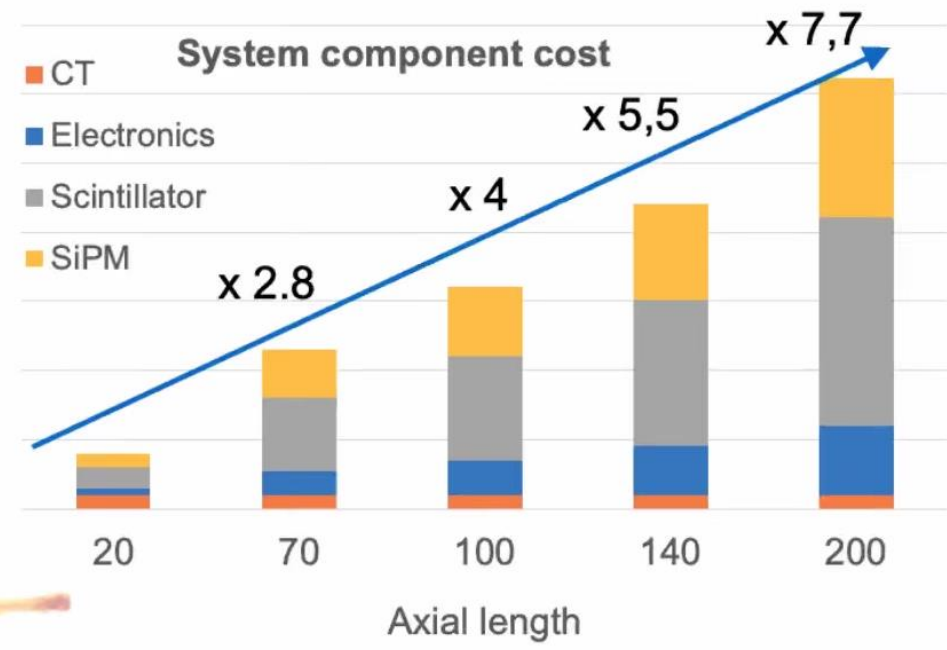
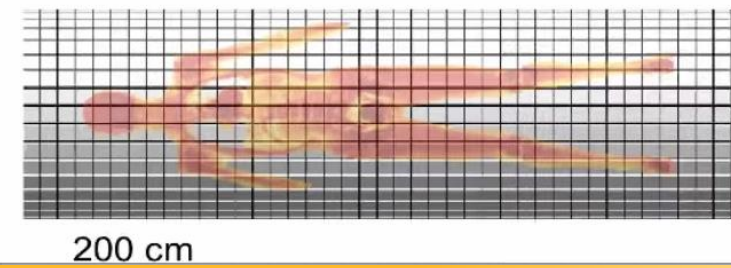
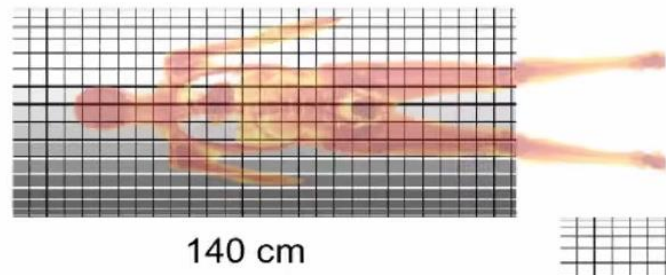
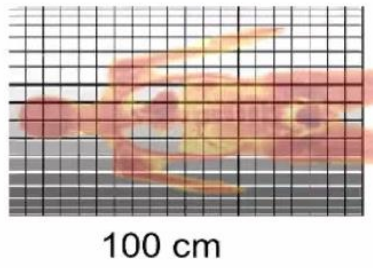
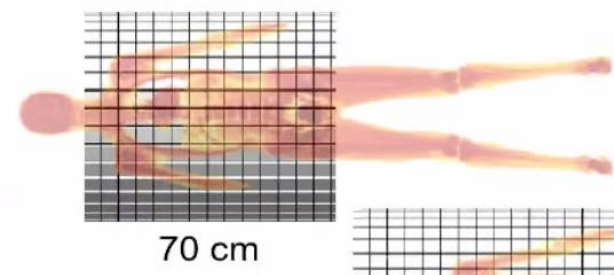
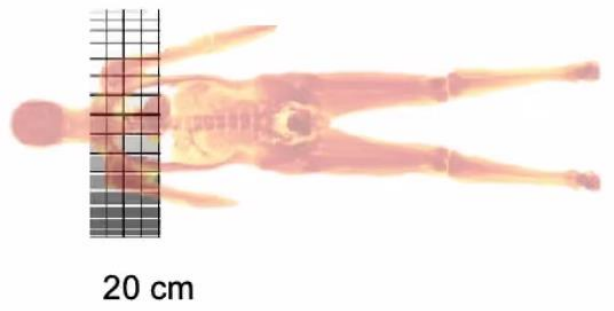
- Increase solid angle coverage

The **EXPLORER** project



~40-fold increase for total-body imaging

Total Body PET cost issue



Standard PET-CT: 2-3 Meuro

TB PET: 8-15 Meuro

Even with a 2x - 3x higher throughput financially difficult for most centers

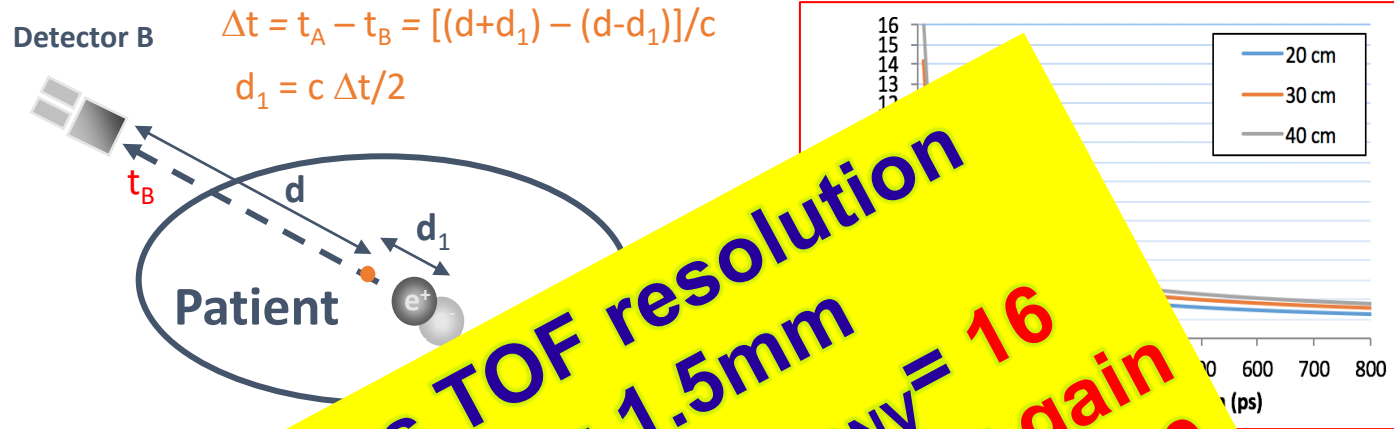
State of the art in total body PET

[Stefaan Vandenberghe](#), [Pawel Moskal](#) & [Joel S. Karp](#)

EJNMMI Physics 7, Article number: 35 (2020) | [Cite this article](#)

5986 Accesses | 6 Citations | [Metrics](#)

Time of Flight PET



10ps TOF resolution
 $\delta x = 1.5\text{mm}$
 $\text{SNR}_{\text{TOF}}/\text{SNR}_{\text{conv}} = 16$
Effective sensitivity gain
 $(\text{SNR}_{\text{TOF}}/\text{SNR}_{\text{conv}})^2/1.47 = 180$

Distance (cm)	SNR	SNR*
20	0.15	16
100	1.5	5.2
200	3.0	3.6
500	7.5	2.3

Biograph Vision

* SNR gain for 40cm phantom

The 10ps challenge: a step toward reconstructionless TOF-PET

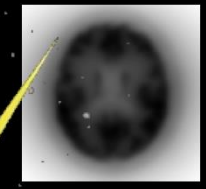
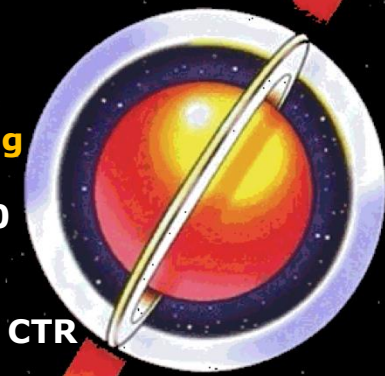
The 10ps challenge:

- a spur on the development of fast timing
- an opportunity to get together
- an incentive to raise funding
- a way to shed light on nuclear instrumentation for medical imaging

One unique challenge launched for 5 to 10 years and operated by an international organisation with rules issued by the community based on the measurement of CTR combined to sensitivity

Several milestones and prizes:

- 3 years after the launch of the challenge: 1M€ expected for the Flash Gordon prizes for the realisation of 3 important milestones
- until the end of the challenge: 1M€ expected for the Leonard McCoy price for the first team meeting successfully the specifications of the challenge



Non-TOF FBP



Non-TOF OSEM



10ps TOF FBP



10ps TOF OSEM

Officially endorsed by

EANM
European association of Nuclear Medicine

EIBIR
European Institute for Biomedical Imaging Research

WMIS
World Molecular Imaging Society

Crystal Clear collaboration
31 Institutions worldwide

+ a number of prestigious individuals

Following an idea of C. Morel in the Crystal Clear collaboration

Image Better

- **> 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

Image Longer

- **200-fold greater dynamic range**

can image for seven more half lives

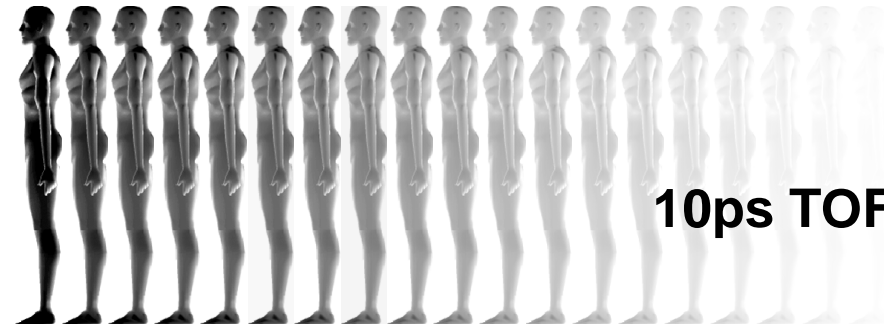
- **^{11}C**
Up to 4 hours

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

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



Conventional PET



10ps TOFPET

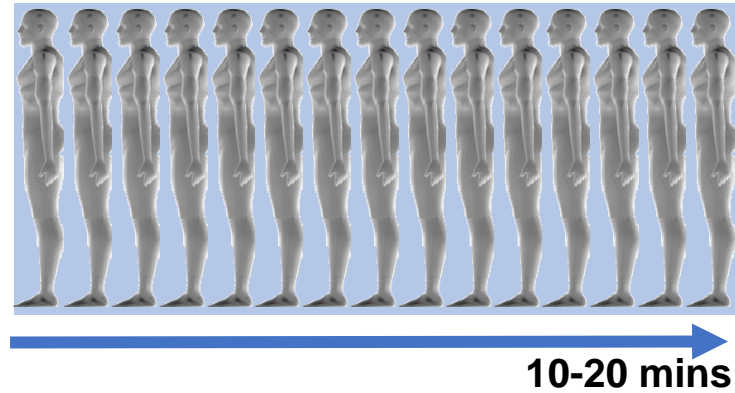
Adapted from S. Cherry, UC Davis

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

Adapted from S. Cherry, UC Davis

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



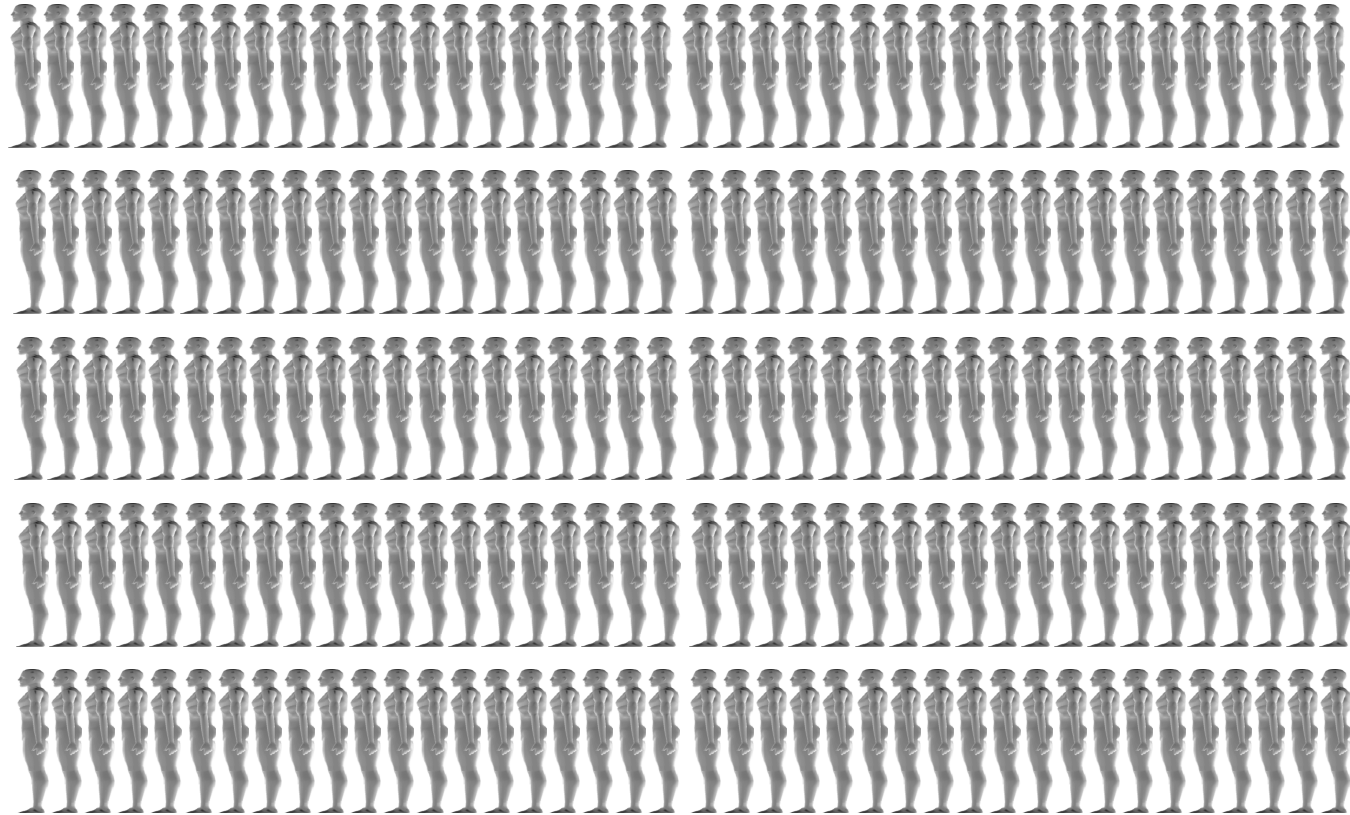
10ps TOFPET

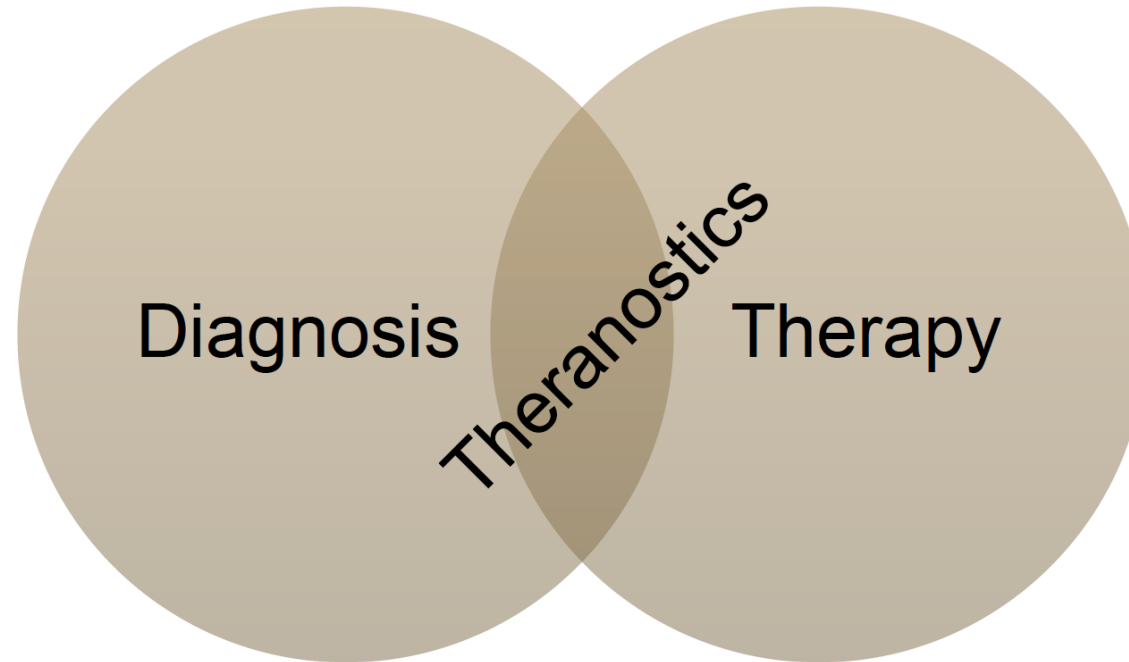
Image More Often

Conventional PET



10ps TOFPET



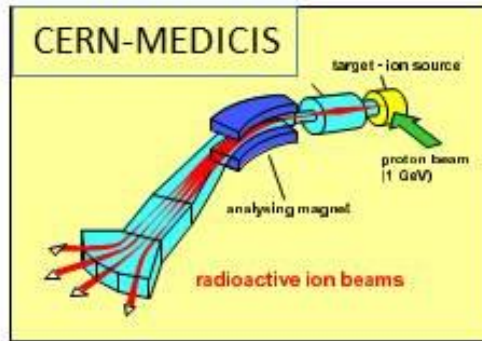


^{68}Ga -PSMA + ^{111}In -PSMA for diagnosis and therapy of prostate cancer

^{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