Application of High-Energy Physics Technologies to PET

(Positron Emission Tomography)

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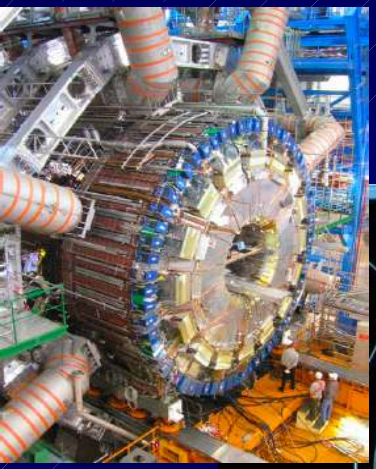
National Science Foundation Visit, June 26, 2007

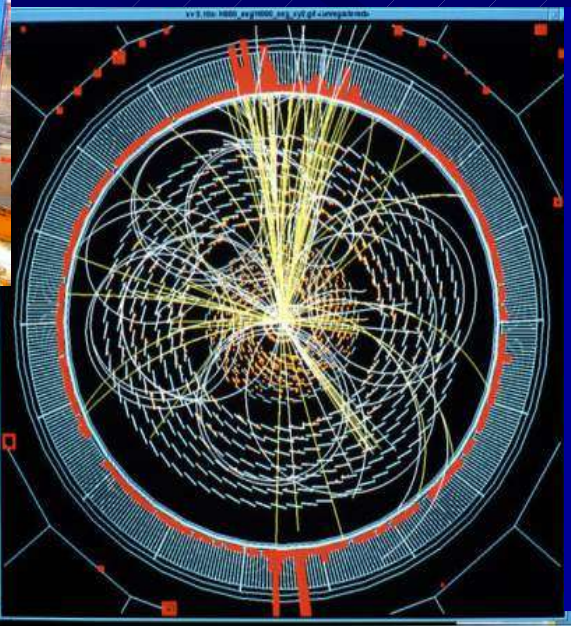
HEP & PET

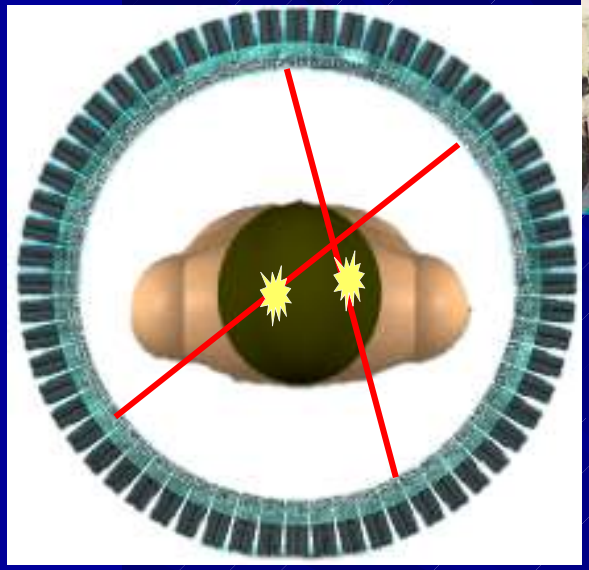
Similarities and differences

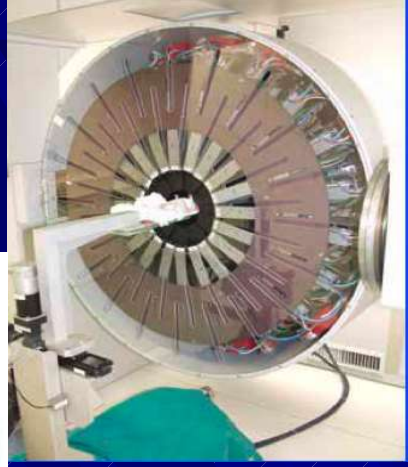


Calorimeter

HEP







PET Scanner

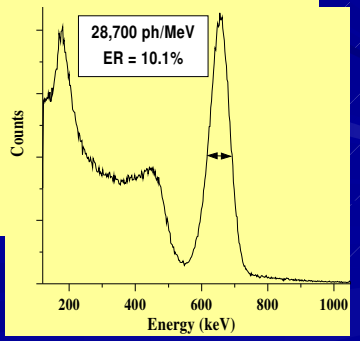
Biomedical Imaging

Similarities

- Geometry and granularity
- Detector (Crystals & scintillator)
- Sensor (PM,APD)
- Electronics:Fast (40 MHz), compact
- Event rate & Data volume (Gbit/s)

Differences

- Energy range (10GeV-511keV)
- No synchronisation
- --> free running electronics
- Multiple vertices



From HEP to Medical Imaging

Where **techniques** are transferred to developments in biomedical field

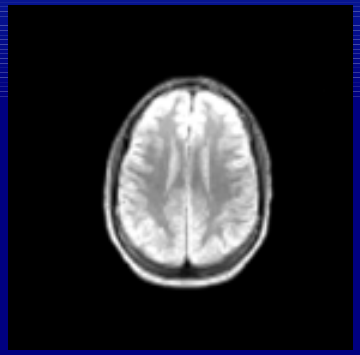
Medical Imaging has so far only partially benefited from new technologies developed for High Energy Physics detectors

- *New scintillating crystals and detection materials*
  - *CMS (WPbO4) Luap …(Crystal Clear col)*
- *Photodetectors : Highly segmented and compact*

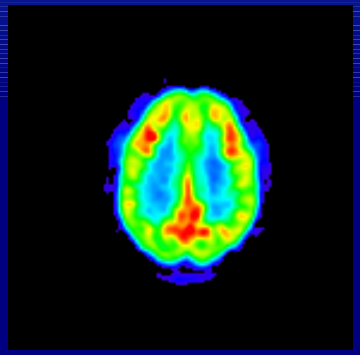
  -- PMT APD SiPM
  - *APD : SSC/SDC (1991) CMS (1996) MicroTEP TEP*
- *Electronics & signal treatemnt Highly integrated*
  - *Fast, low noise,low power preamp*
  - *Digital filtering and signal analysis*
- *Trigger/DAQ*
  - *High level of parallelism and event filtering algorithms*
  - *Pipeline and parallel read-out, trigger and on-line treatment*
- *Simulation & Computing*
  - *Modern and modular simulation software using worldwide recognized standards (GEANT)*

PET: Molecular Imaging of Life and Life Processes

Live Brain t 1

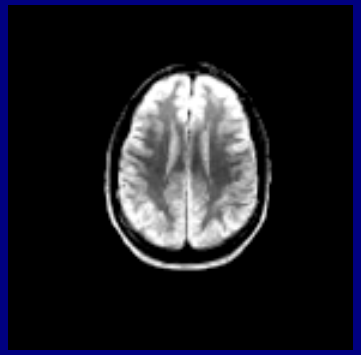


M R



P E T

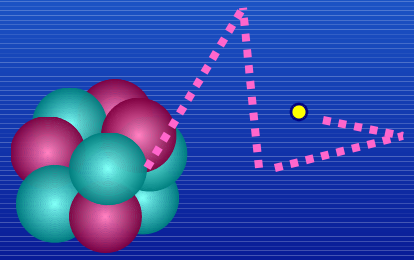
Dead Brain t 2



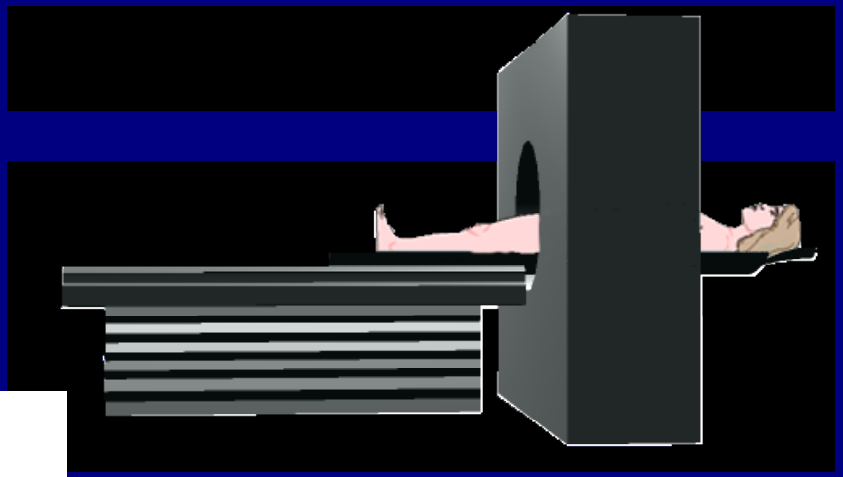
M R

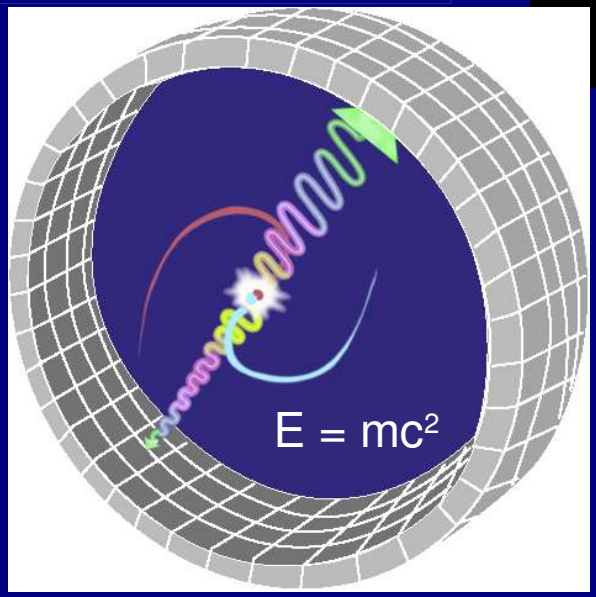
P E T

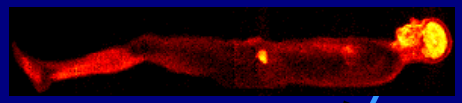
PET Principle



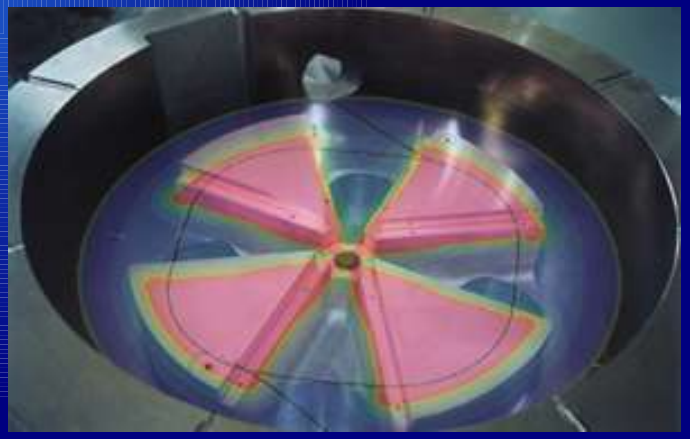
$P \rightarrow N + e^{+} + n + \text{energy}$

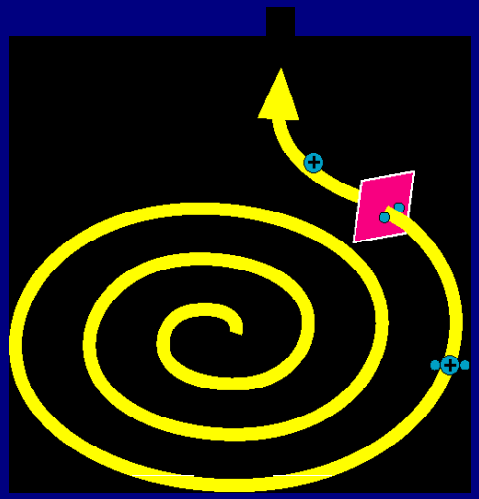


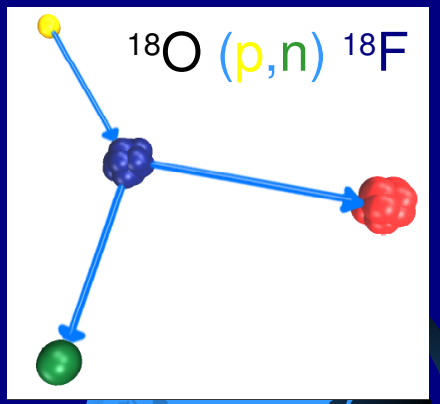




Production of Isotopes
(Mini-Cyclotron)







PET Isotopes

^{15}O

^{13}N

^{11}C

^{18}F

^{64}Cu

^{82}Rb

^{124}I

PET Tracers

$[^{15}O]$-O_2 $[^{15}O]$-H_2O

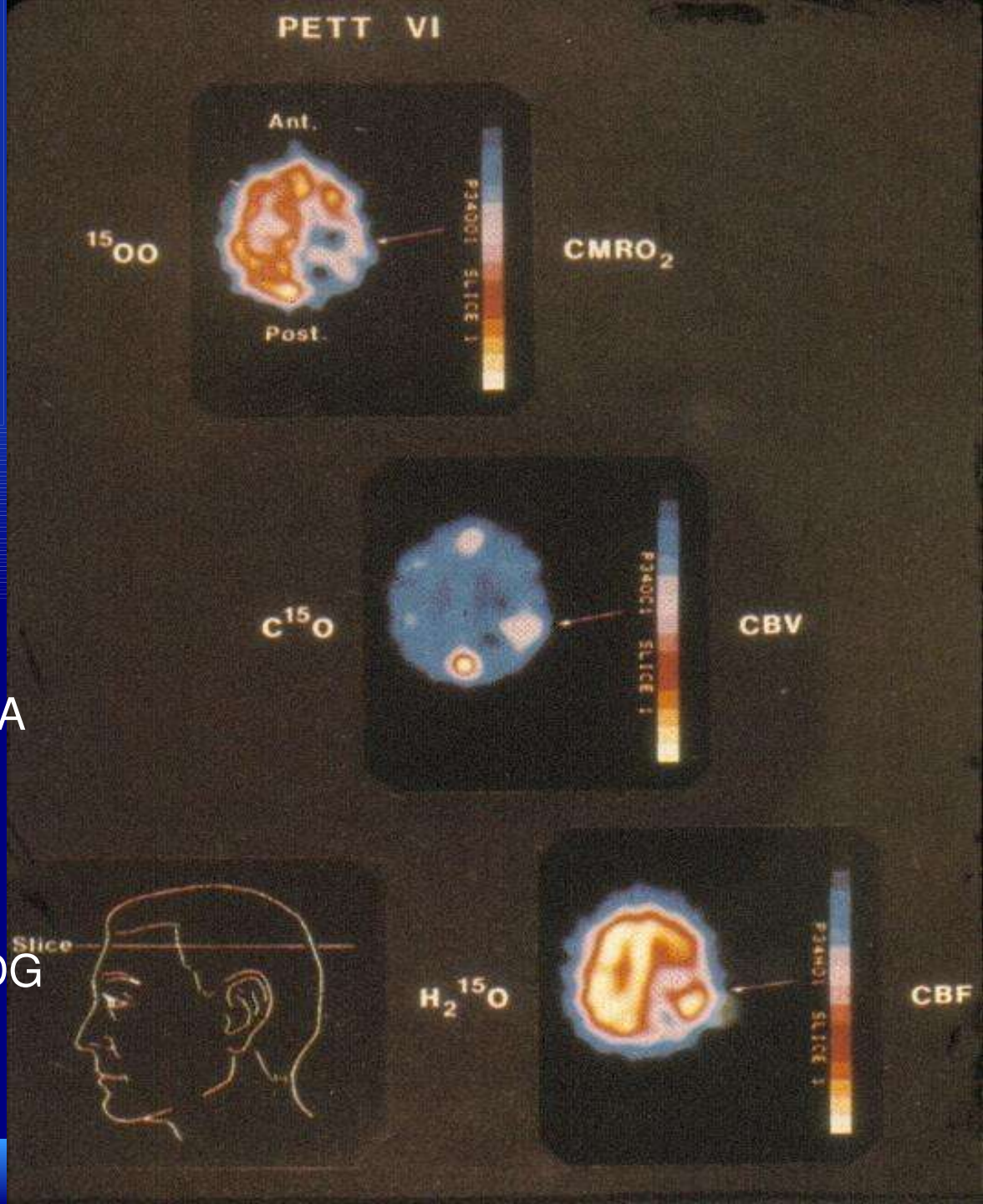
$[^{15}O]$-H_2O $[^{15}O]$-CO

$[^{13}N]$-NH_3 $[^{18}F]$-FDOPA

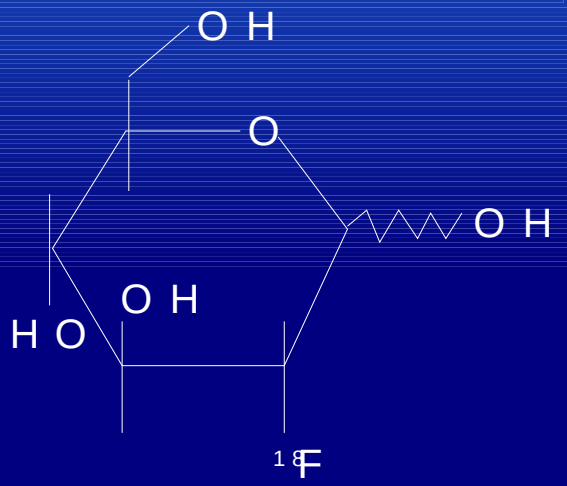
$[^{13}N]$-glutamate $[^{18}F^-]$

$[^{11}C]$-acetate $[^{18}F]$-FDG

$[^{11}C]$-palmitate



^{18}Fluoro-2-deoxy-D-glucose



[^{18}F]–FDG

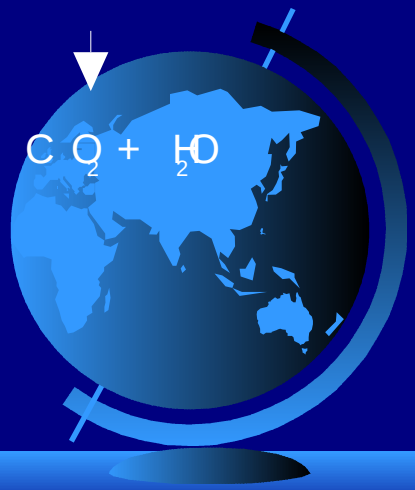
PLASMA

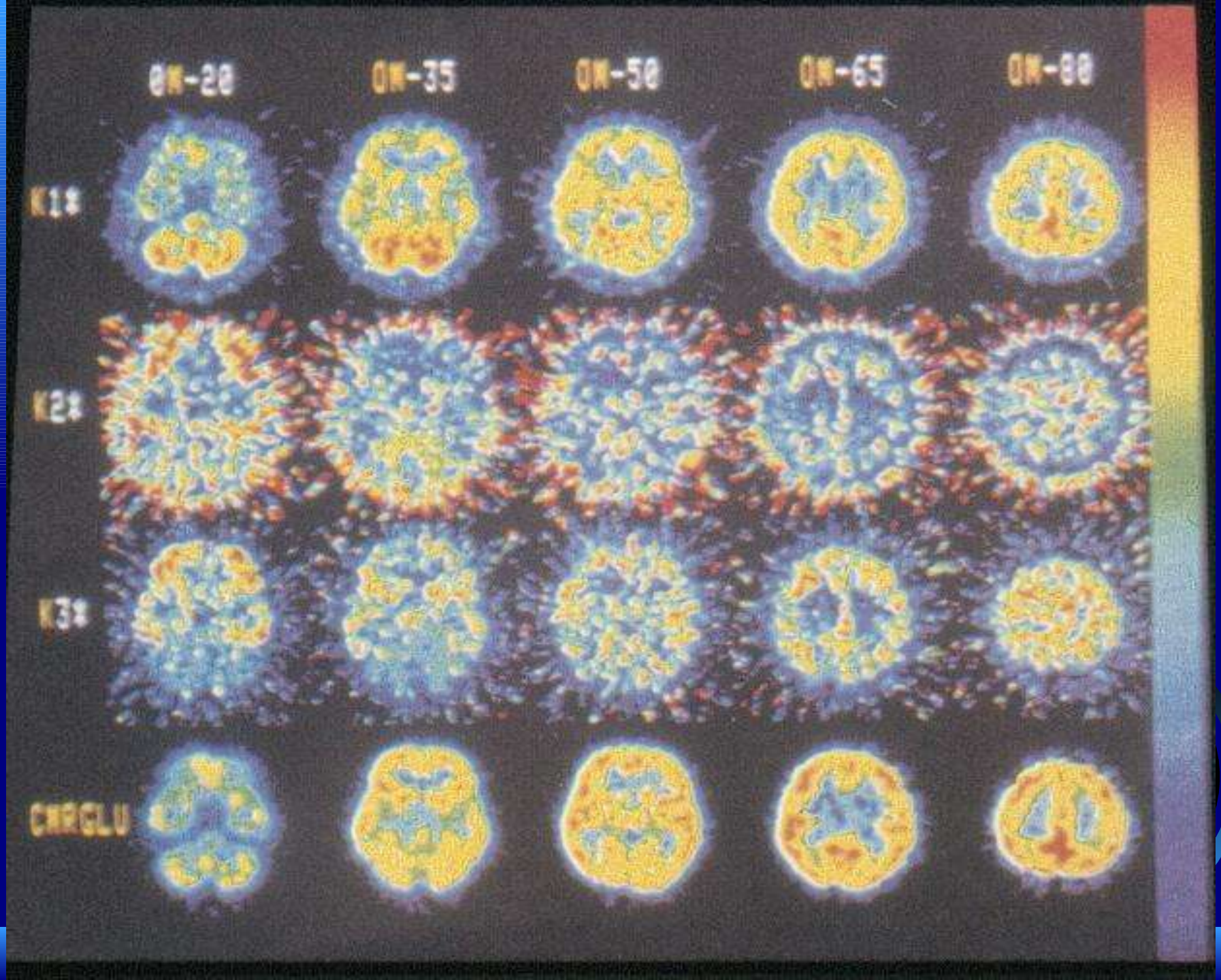
TISSUE

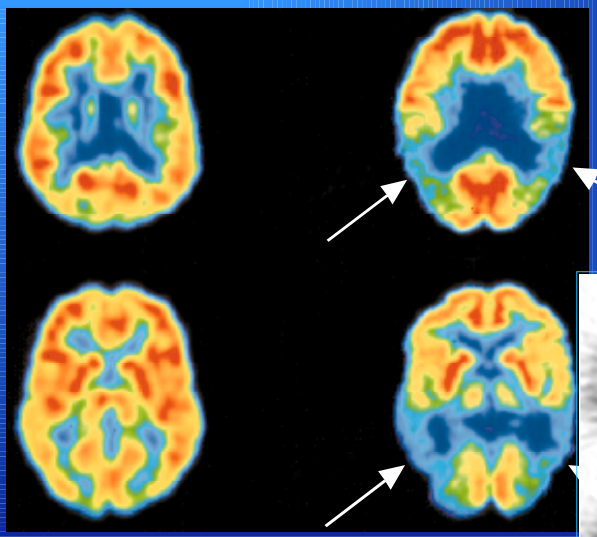
FDG ⟷ FDG FDG–6–P

glucose ⟷ glucose glucose–6

$CO_2 + H_2O$

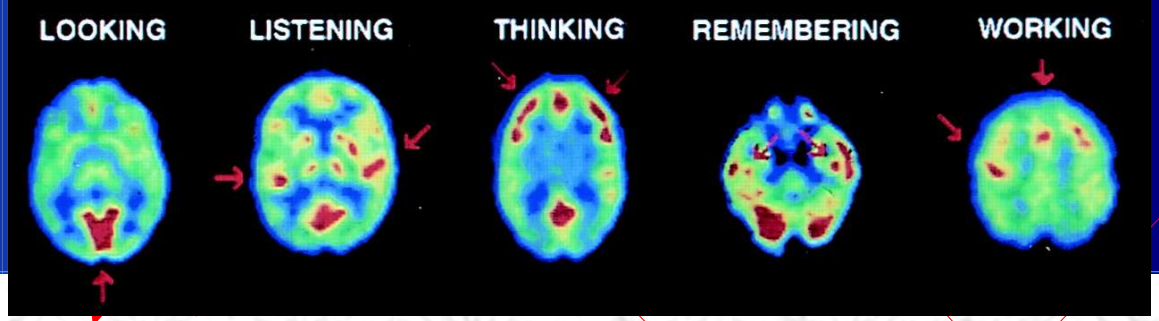



ON-20
ON-35
ON-50
ON-65
ON-80
K1*
K2*
K3*
CMRGLU

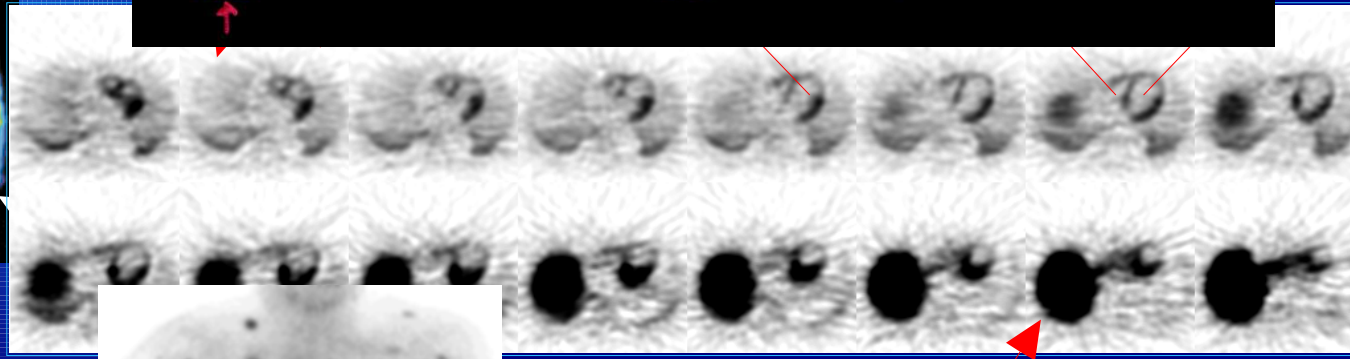


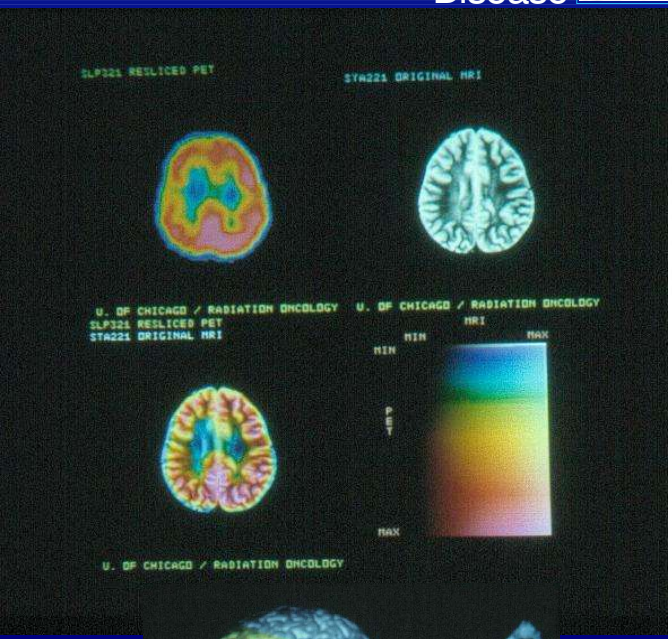
Normal

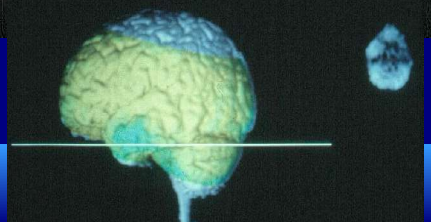
Alzheimer' Disease

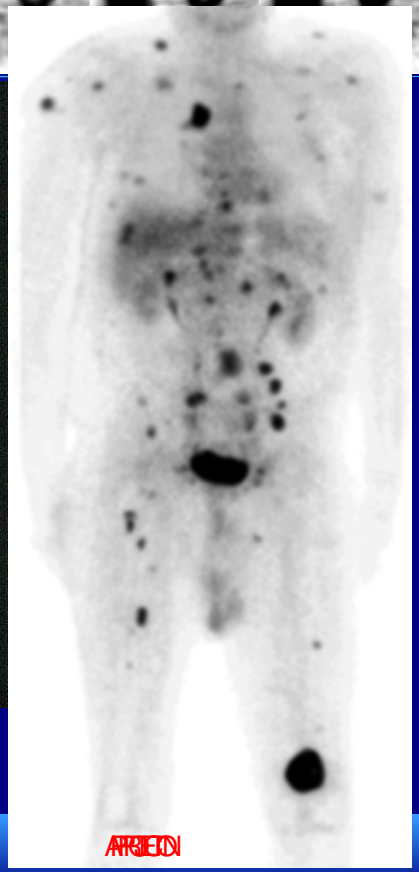


LV

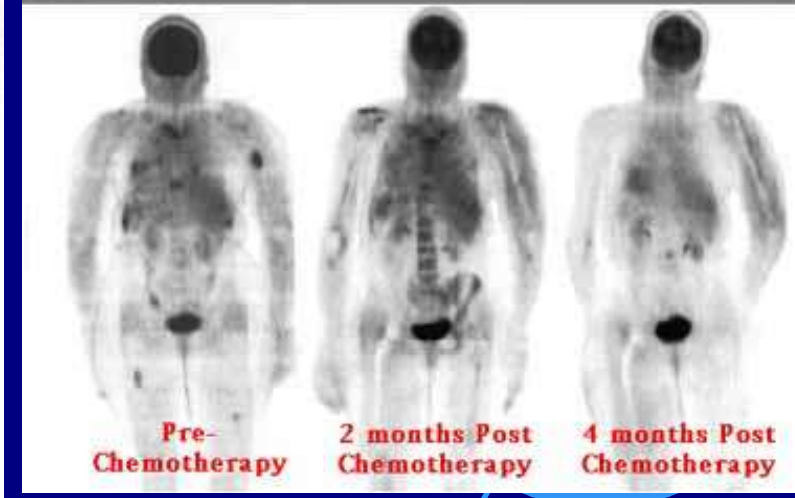




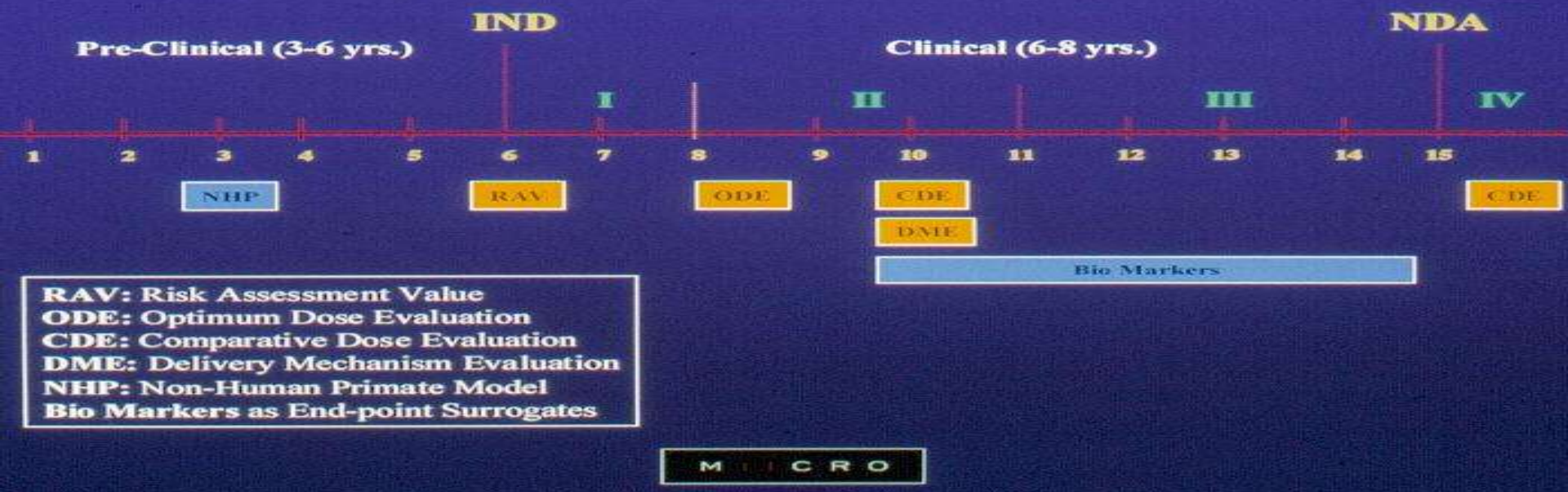




Whole Body PET Study using ^{18}FDG (^{18}F-fluorodeoxyglucose)--60 minutes



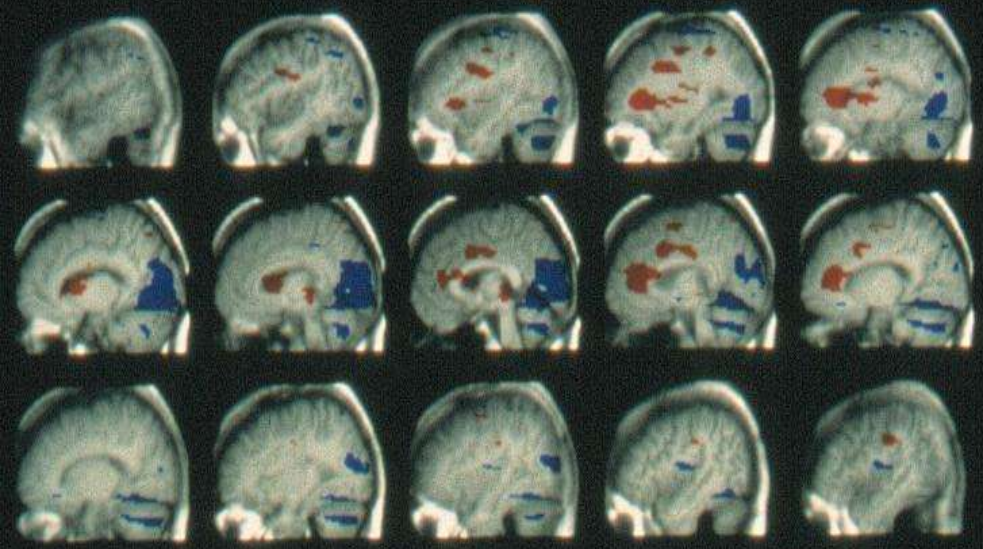
MICRO Neuro-Solutions



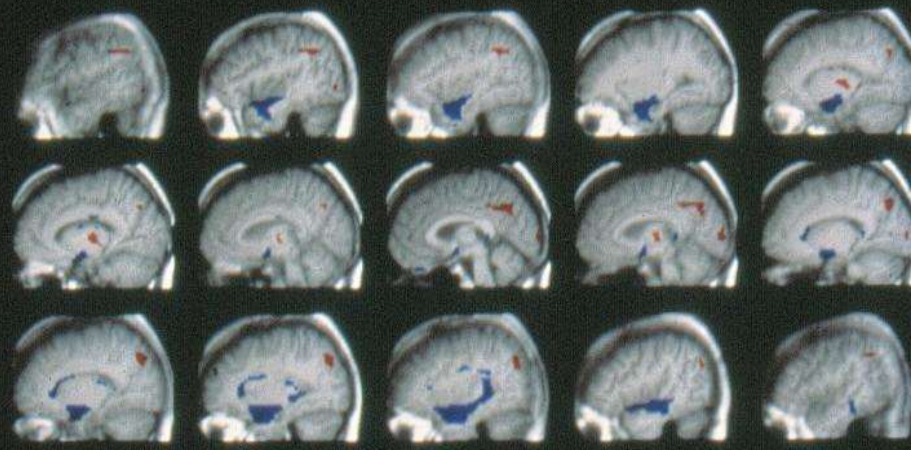
RAV: Risk Assessment Value
ODE: Optimum Dose Evaluation
CDE: Comparative Dose Evaluation
DME: Delivery Mechanism Evaluation
NHP: Non-Human Primate Model
Bio Markers as End-point Surrogates

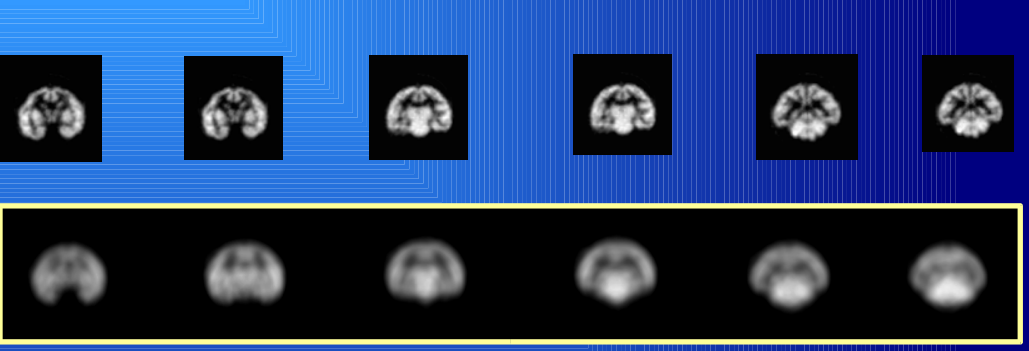
MICRO

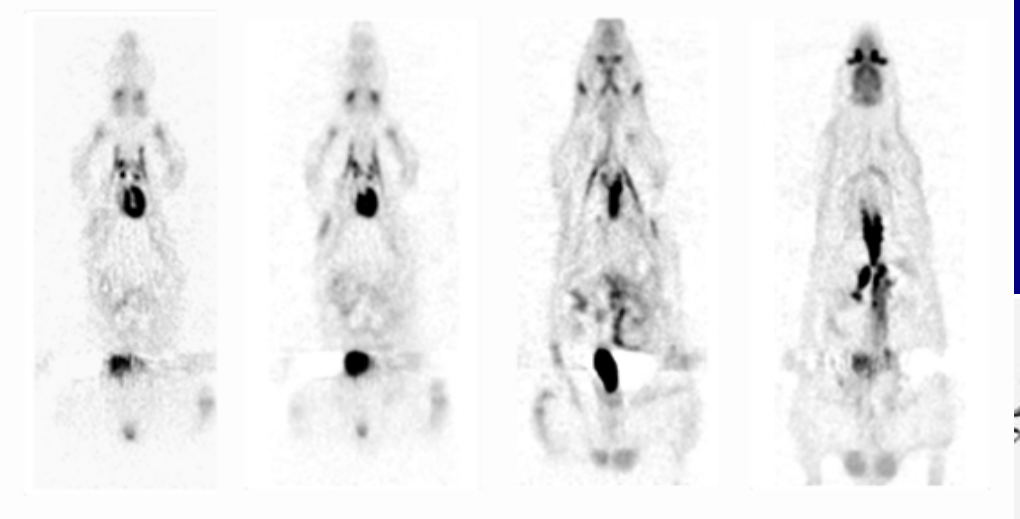
Effects of ethanol on rCMglu

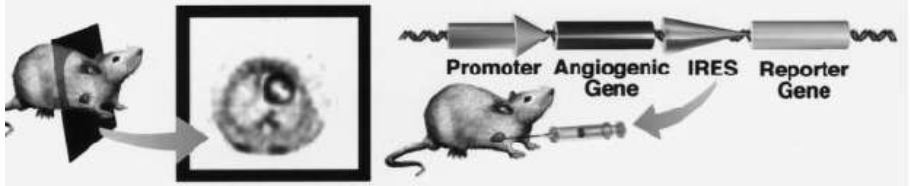


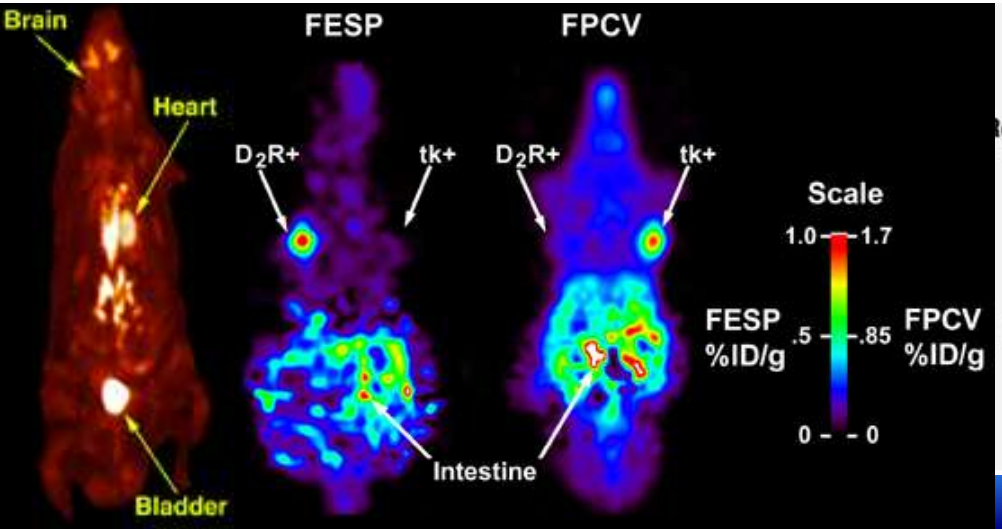
Effects of fluoxetine on rCMglu

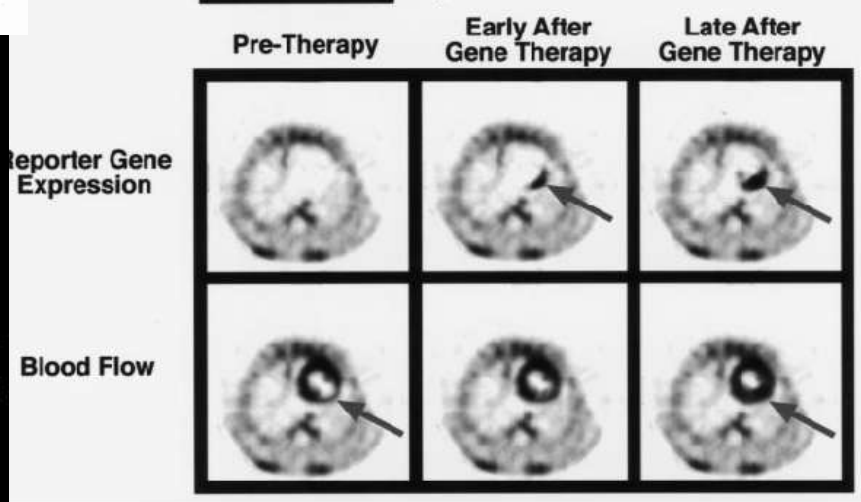




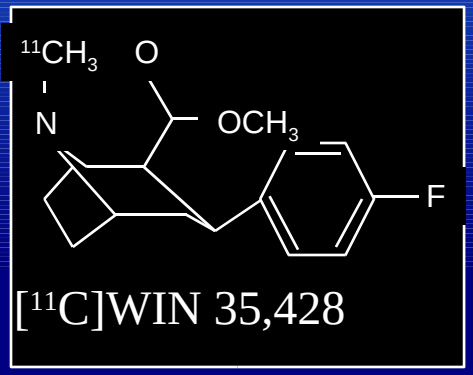



Promoter
Angiogenic Gene
IRES
Reporter Gene

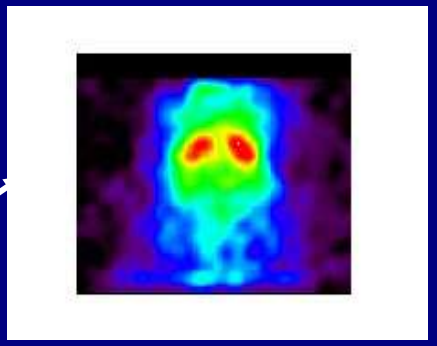

Brain
Heart
Bladder
FESP
FPCV
D2R+
tk+
D2R+
tk+
Intestine
Scale
1.0
1.7
FESP %ID/g
.5
.85
FPCV %ID/g
0
0

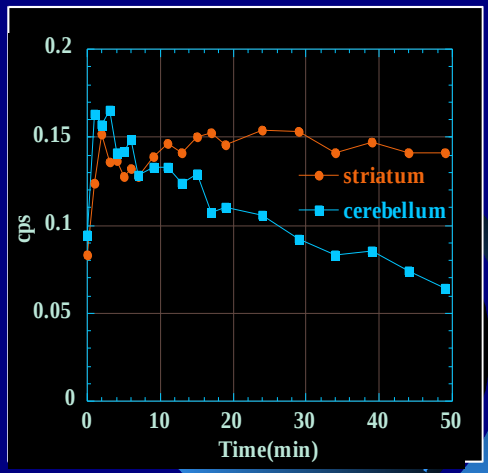

Pre-Therapy
Early After Gene Therapy
Late After Gene Therapy
Reporter Gene Expression
Blood Flow

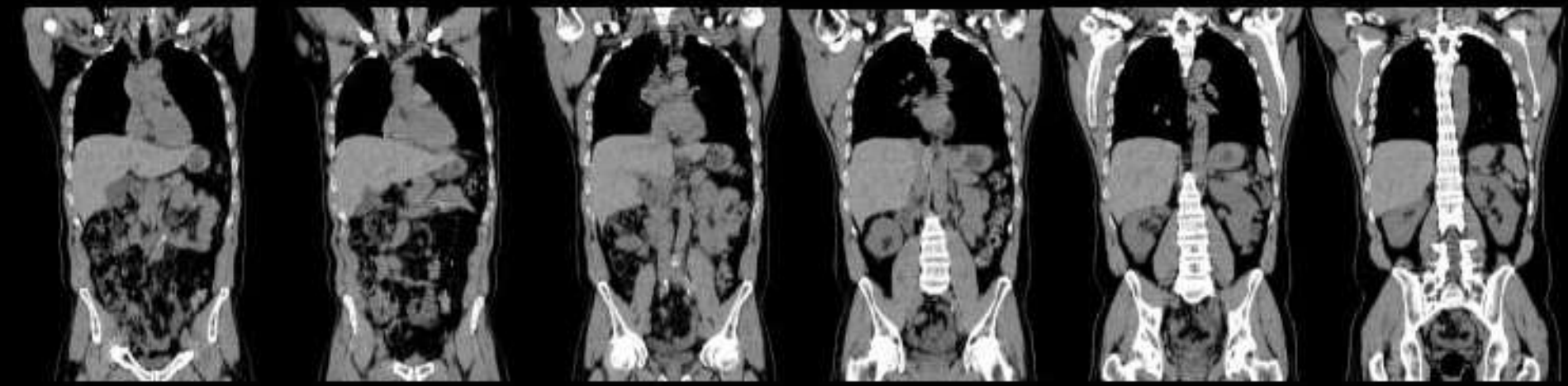
Biochemical Imaging with Small Animals

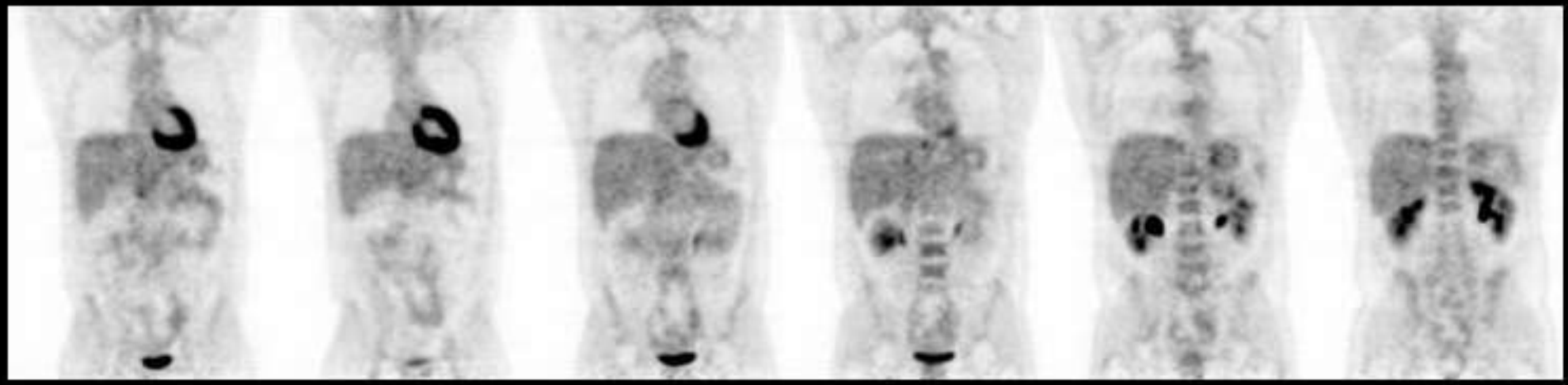


microPET









Human PET: 3-4mm; Target: 1mm

Animal PET: 1-2 mm; Target: <0.5mm

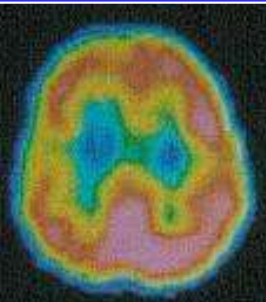
Fast Dynamic Image Acquisition

High Resolution & High Sensitivity

High-Performance & Low-Cost (HPLC)

Multi-Modality Image Integration

Fusion of PET & MRI



U. OF CHICAGO / RADIATION ONCOLOGY U
SLP321 RESLICED PET
STA221 ORIGINAL MRI

ICAGO / RADIATION ONCOLOGY

Chicago Tribune

Final Edition

$1.25 Sunday, May 8, 1988

Mysteries of the brain being revealed

By Ronald Kotulak
Science Writer

The brain is the body's last and greatest mystery, but it is beginning to yield its fabulous secrets.

Scientists are discovering the biological bases for mental disorders and are working on ways to actually see thoughts, raise IQs, improve memory and alter the 3-pound organ in ways not yet dreamed of.

Already new findings about the causes of mental illness have had a dramatic impact on the mentally ill, not only leading to new treatments but also easing the stigma by shifting the blame from the victim to brain chemistry—and thus encouraging more people to seek help.

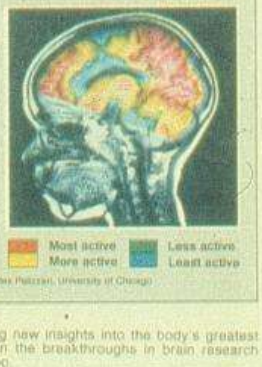
But even bigger payoffs are looming as scientists develop ways to attack some of the brain's most common disorders—injury, mental retardation, learning and memory problems, stroke, Alzheimer's disease, Parkinson's disease, schizophrenia and aggressive tendencies.

The new era in brain research is being accelerated by an explosion in molecular biology that is enabling scientists to take the brain apart piece by piece and put it back together to learn how it works. With their new tools scientists are able to:

● Peer inside the brain with marvelous imaging devices. For the first time, it is possible to see what areas

New view of the living human brain

PET scan color-coded by computer



Most active
More active
Less active
Least active

Imaging technique: A side view of the brain of a 10-year-old girl suffering from focal encephalitis shows in a single image both the detailed structure and function of the brain. The computer technique, pioneered at the University of Chicago, combines in one image two separate tests. One test uses magnetic fields to make images of internal structures. A second test measures the brain's metabolic activity.

Test results: The combined image shows an infection at the top of the patient's brain that is paralyzing a foot. The yellow patch with a green core in an area that should be all red indicates infection.

Chicago Tribune Graphic; Source: Dr. Charles Pelizzari, University of Chicago

Scientists are achieving startling new insights into the body's greatest mystery. A series of articles on the breakthroughs in brain research begins today, here and in Tempo.

a hamburger, performs a math problem, is sexually aroused, or suffers an anxiety attack.

● Replace parts of the brain. Embedded with their success in animals, researchers are turning to human brain tissue implants in the hope of conquering Parkinson's disease, Huntington's disease and, per-

● Probe the mind's secret for controlling the body. Tantalizing evidence that the brain and body are more profoundly interconnected than expected may outline the link between stress and disease and, conversely, uncover ways that the mind can be used to heal the body.

● Explore the mystery of learning and memory. Using powerful new technology, researchers can trace brain chemicals and neural pathways responsible for thoughts.

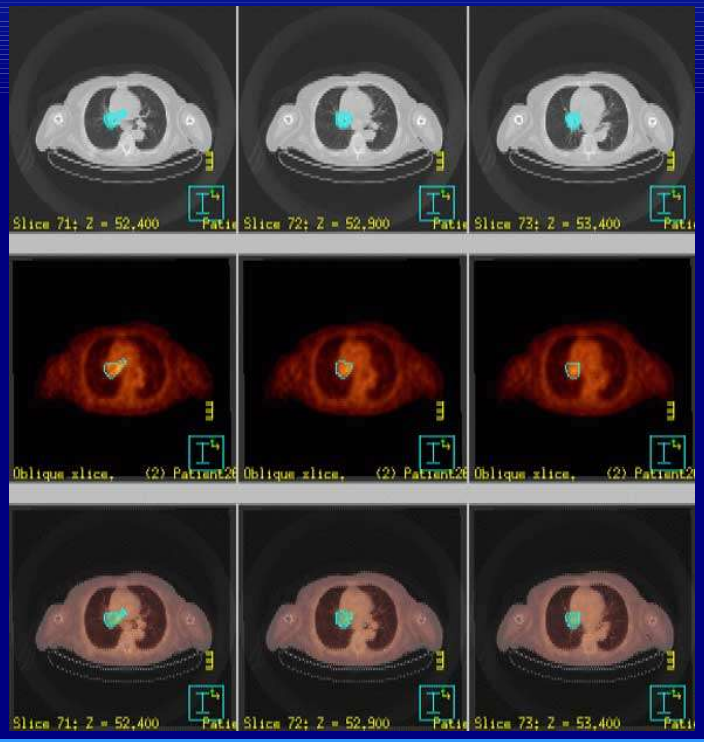
● Develop new treatments for such mental disorders as depression—which, because of recent advances in drugs and therapy techniques, can now be treated successfully in 9 out of 10 patients. One in 5 Americans suffers from a diagnosable mental disorder.

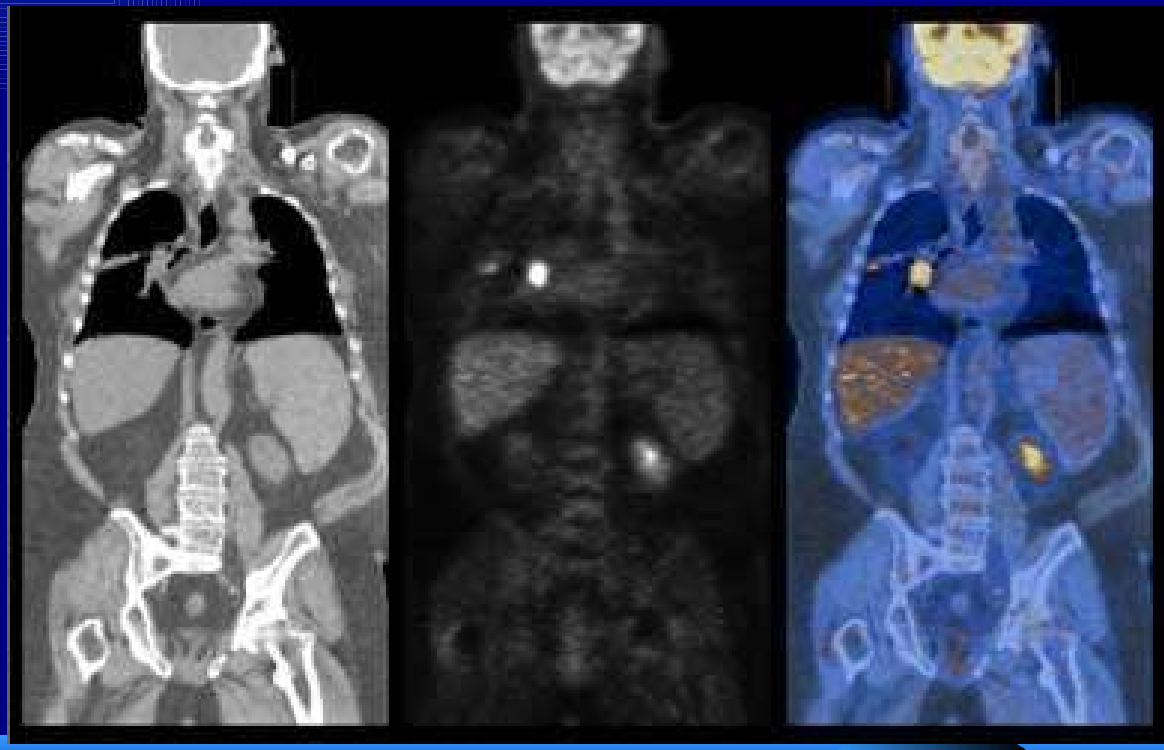
The neuroscience gold rush is largely due to the growing conviction that asking the brain to understand itself is no longer an unsolvable conundrum. Still, it is the most formidable challenge ever undertaken by science.

"The magical days are here," says Eric Kandel, a Columbia University neurobiologist.

"I've always felt that there's just no reason why we can't understand the brain. We're going to get a general view of what we mean when we say a mental process, or we perceive something, or we store information

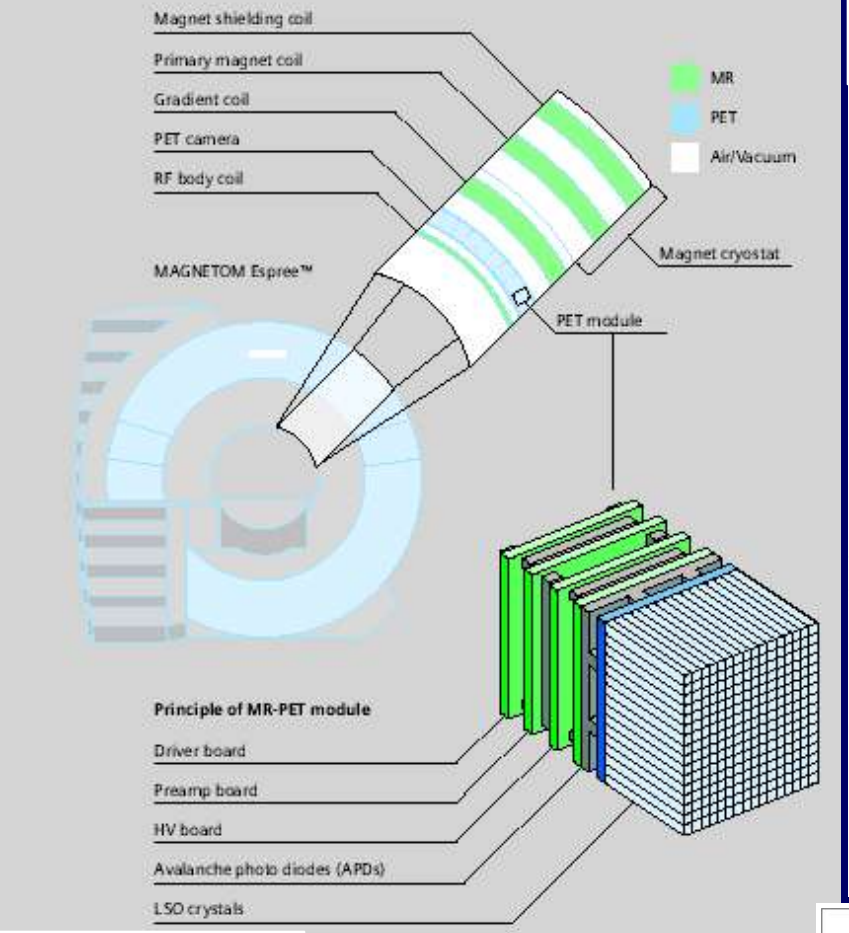
PET/CT Imaging



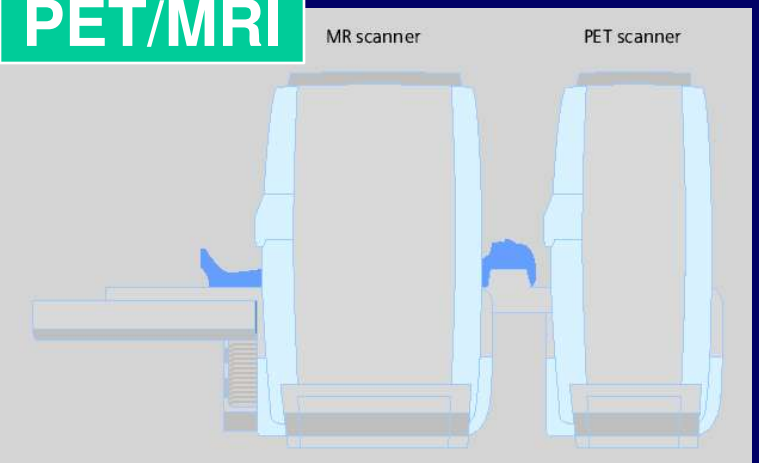


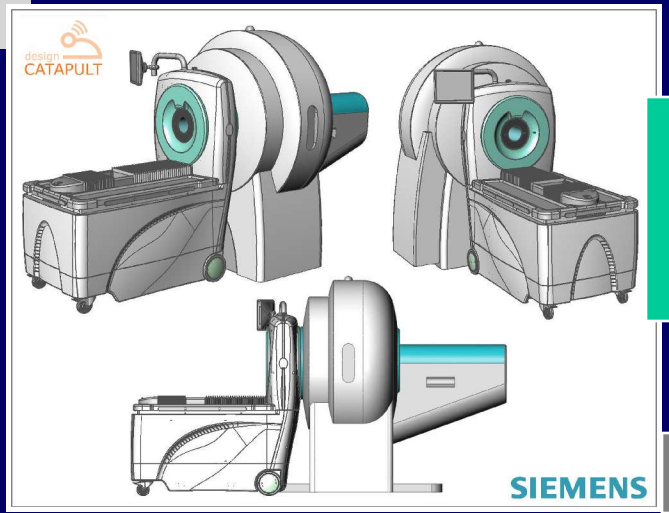
Multi-Modality Integrative System

PET/SPECT



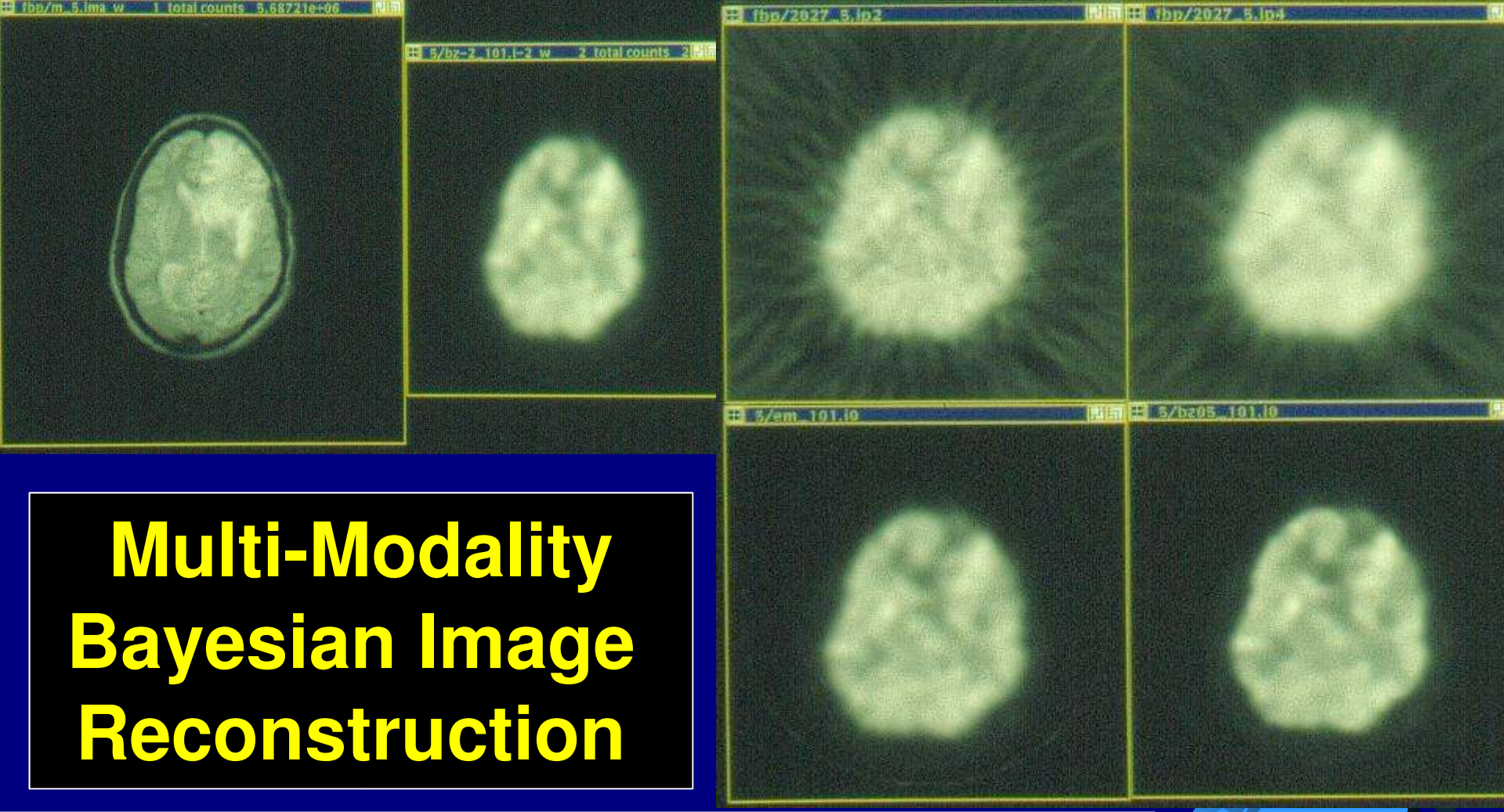
PET/MRI





PET/SPECT/CT
For
Animal Imaging

Siemens “Molecular Imaging”



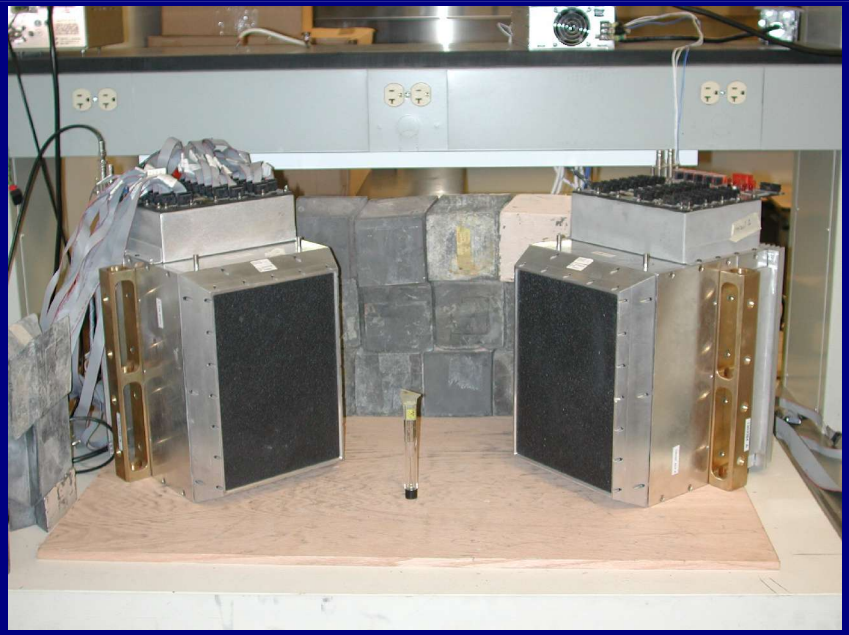
Multi-Modality Bayesian Image Reconstruction

1. Co-registration of PET/SPECT with CT/MRI
2. Incorporation of high-resolution information from the co-registered CT/MR images into a Bayesian image reconstruction framework to enhance image quality of PET/SPECT
5. Using the co-registered CT/MR images as an anatomic map in correction for attenuation and scatters in PET or SPECT

Upper Two:
Filtered BackProj.
Lower Two:
Multi-Modality
Image Reconstru.

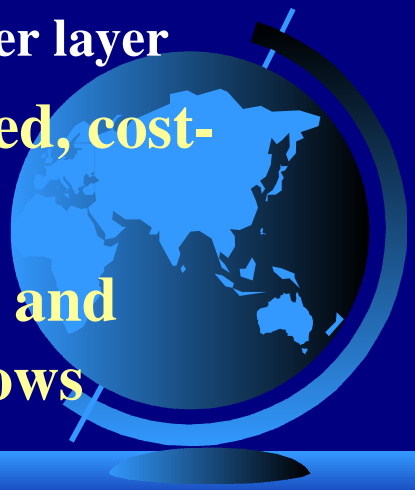
Chen, Kao, et al

A Benchtop Prototype for High-Throughput Animal Imaging

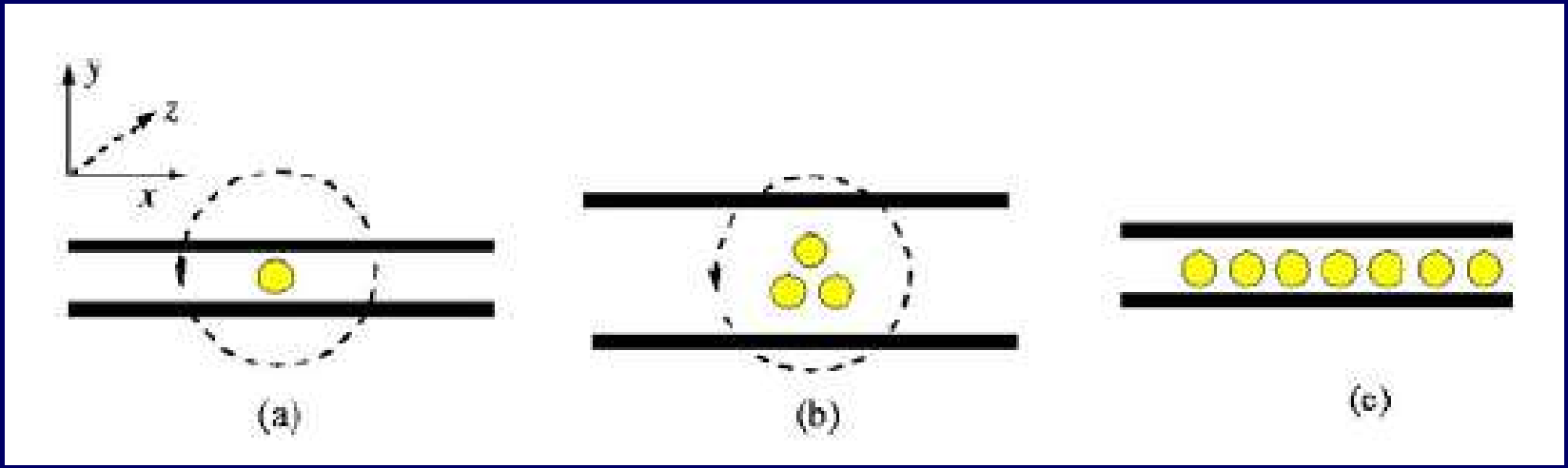


HRRT modules

- LSO crystals with DOI capability
  - good spatial resolution
    - ~2.42mm crystal pitch
    - ~10mm DOI resolution
  - good detection sensitivity
  - high count rate
- large detection sensitive area
  - ~25.2cm ×17.4cm
  - 72×104 crystals per layer
- off-shelf, well tested, cost-effective design
- adjustable energy and coincidence windows

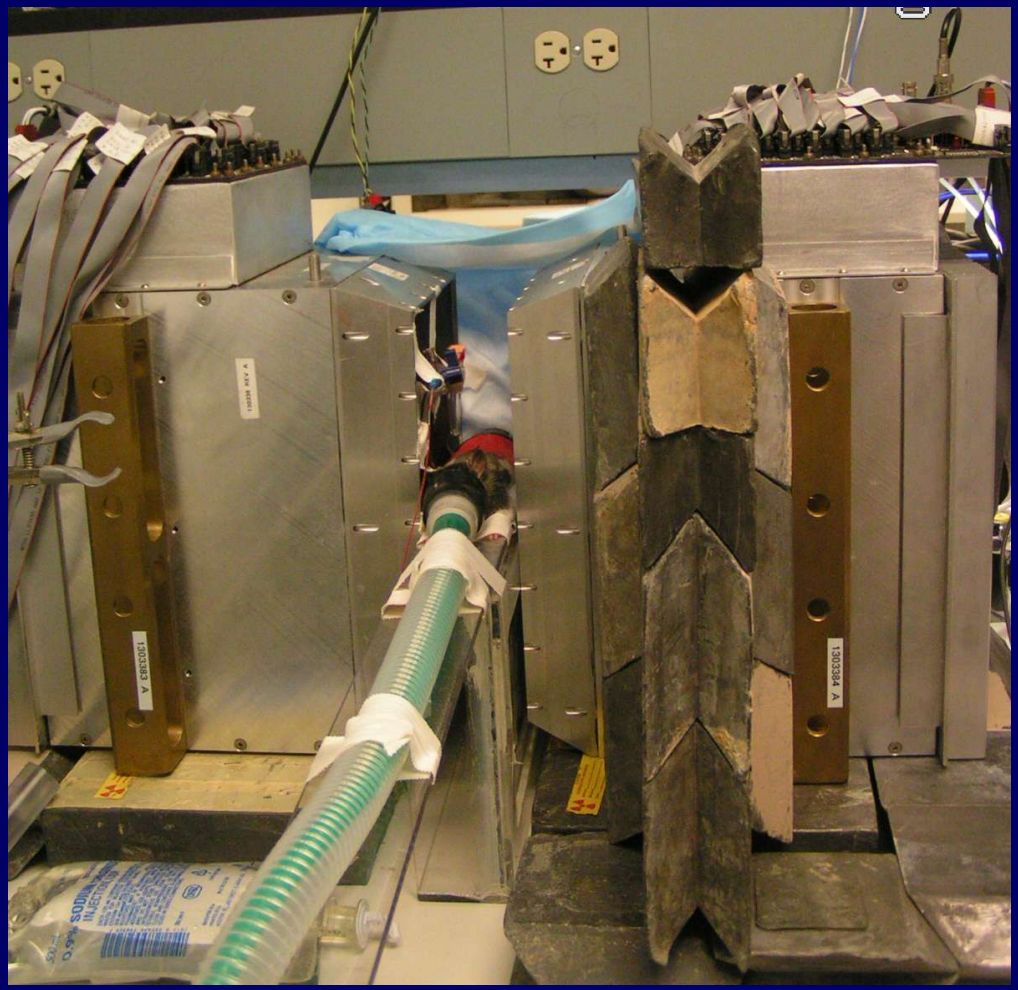


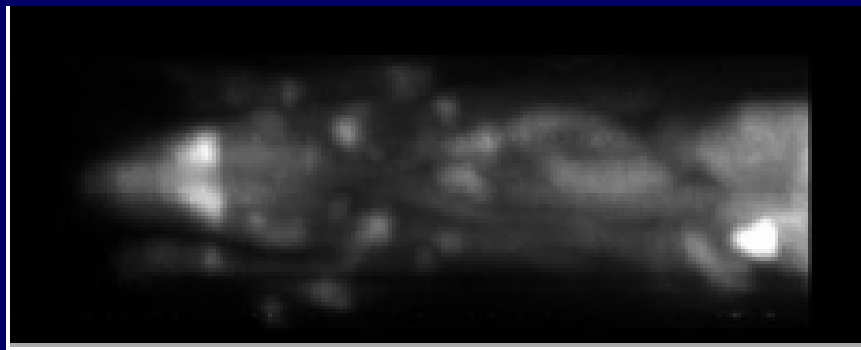
Flexible Configuration

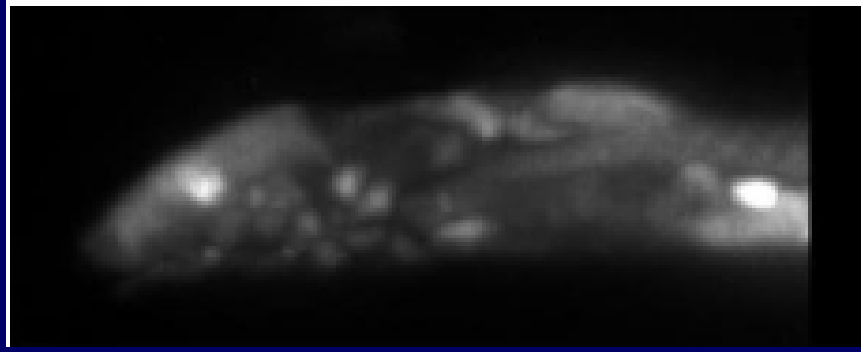


Fully 3D Reconstruction without Angular Rotation

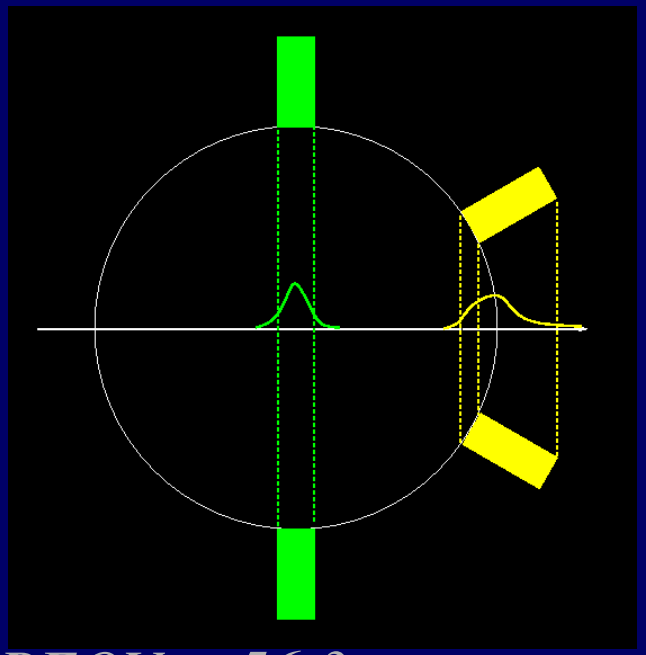
Stationary Compact Dual-Panel PET with Very High Sensitivity

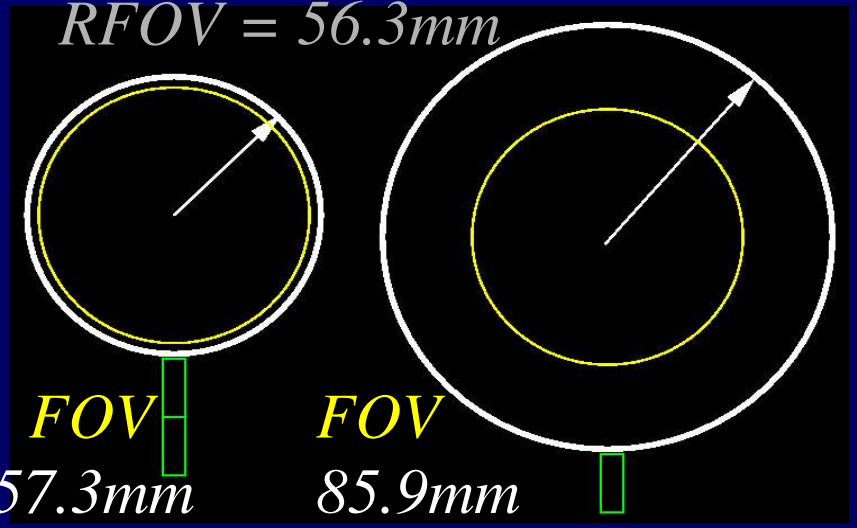


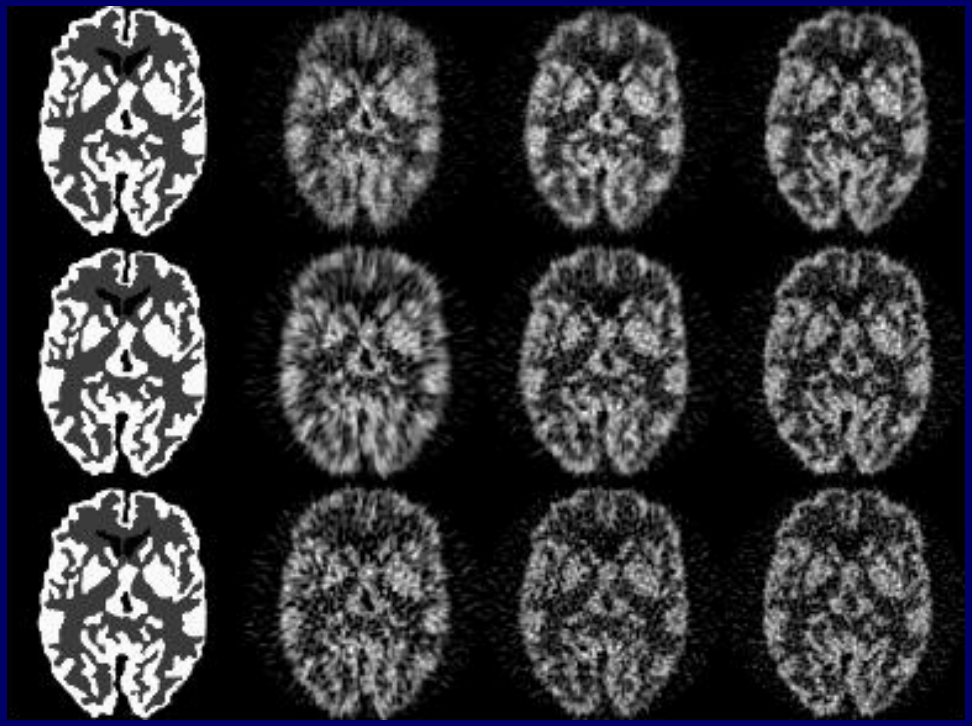




High-Throughput Compact PET





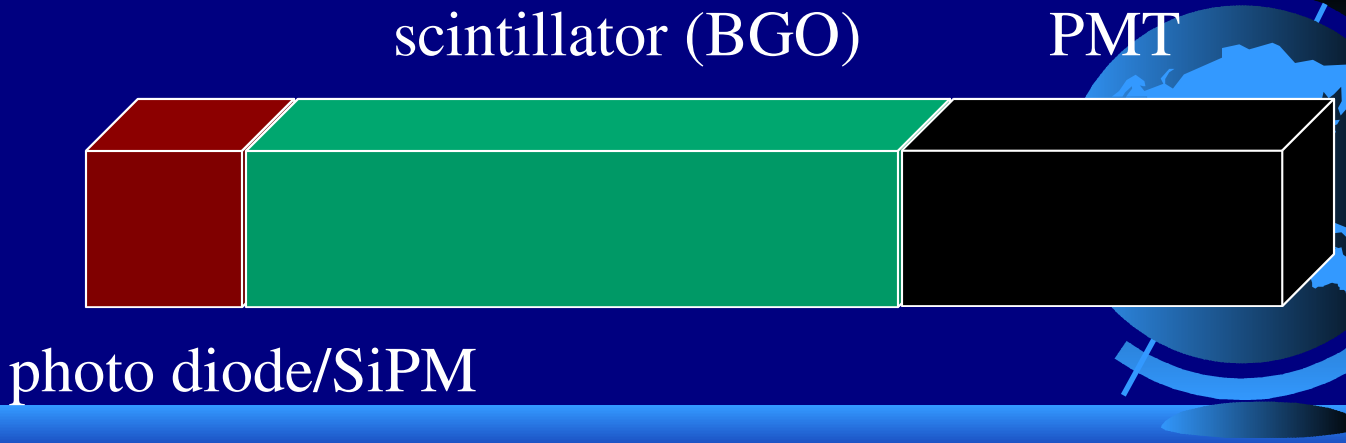


True | Compact, no PSF | Convent'l scanner | Compact, with PSF

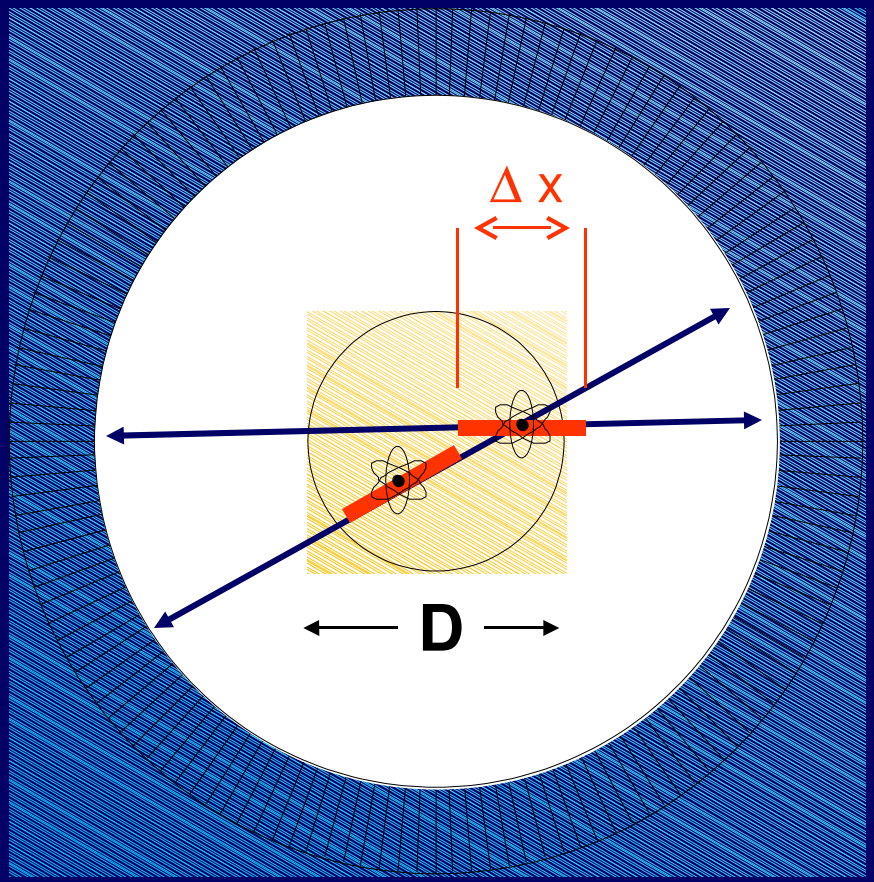
DOI Detectors

- **Phoswich detectors**

- **photo-diodes (or SiPM/MPPC)**



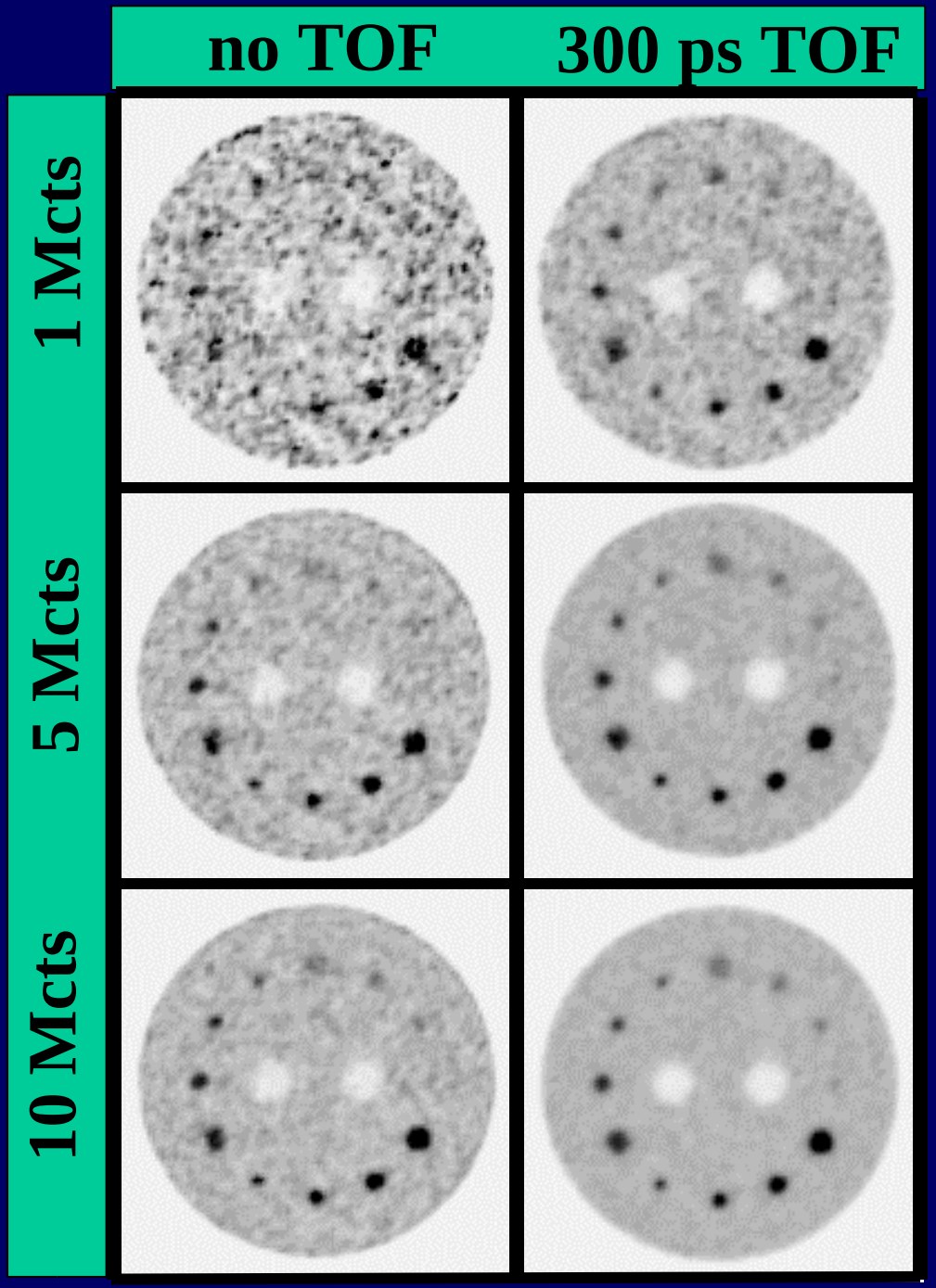
Time-of-Flight Tomograph



- Can localize source along line of flight - *depends on timing resolution of detectors*
- Time of flight information can improve signal-to-noise in images - *weighted back-projection along line-of-response (LOR)*

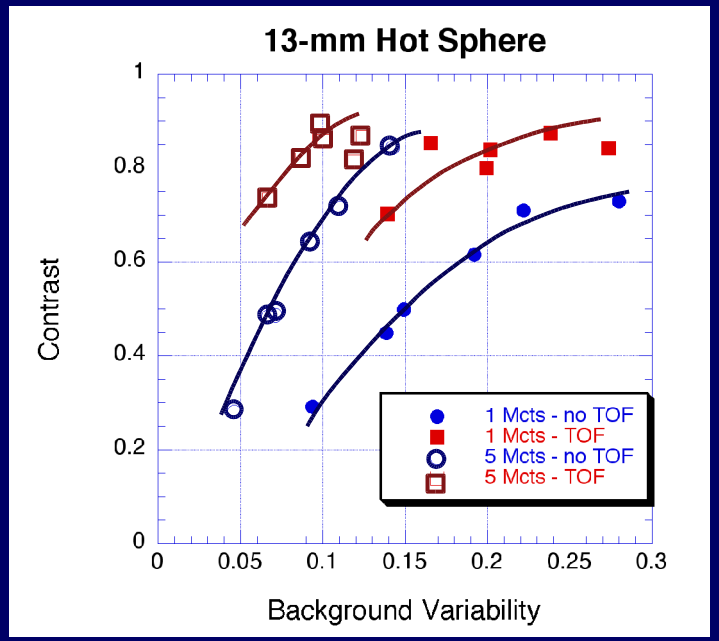
Δx = uncertainty in position along LOR

$= c \cdot \Delta t/2$



Benefit of TOF

Better image quality
Faster scan time



Karp, et al, UPenn

TOFPET DREAM

PET without TOF (>99%)

One Commercial TOFPET System Available

with 750 picosec TOF (11.25 cm LOR Resolution)

30 picosec TOF

4.5 mm LOR Resolution

10 picosec TOF

1.5 mm LOR Resolution

3 picosec TOF

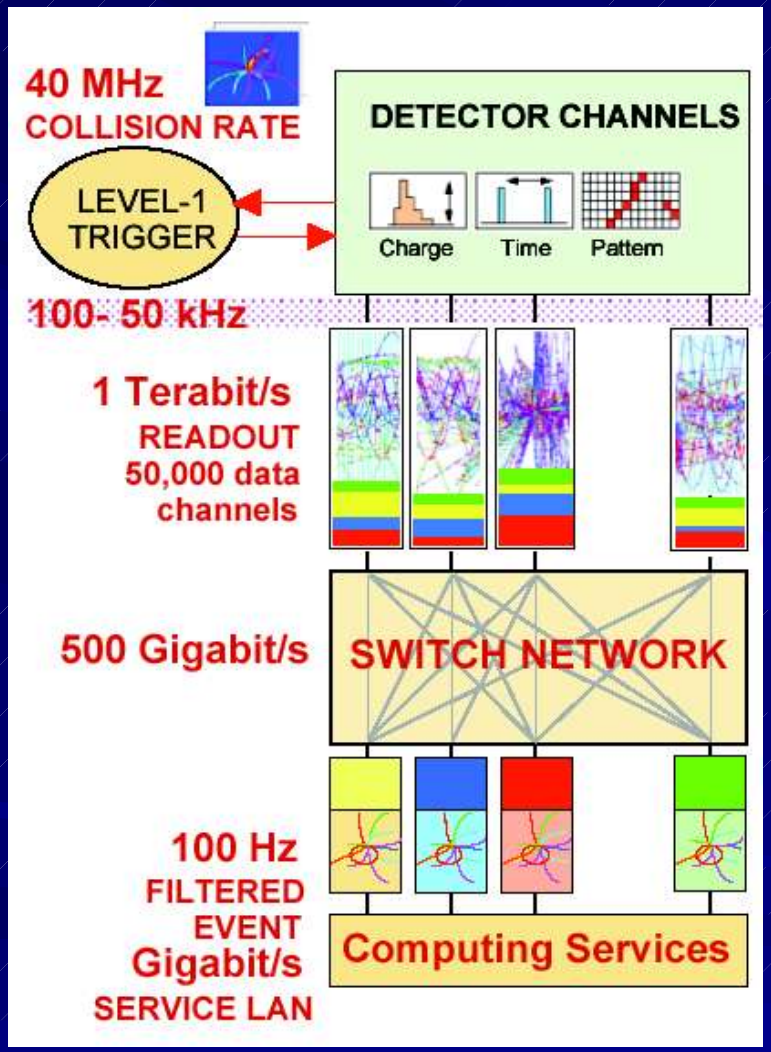
0.45 mm LOR Resolution

Histogramming

No “Image Reconstruction”

Pipeline Architectures

LHC

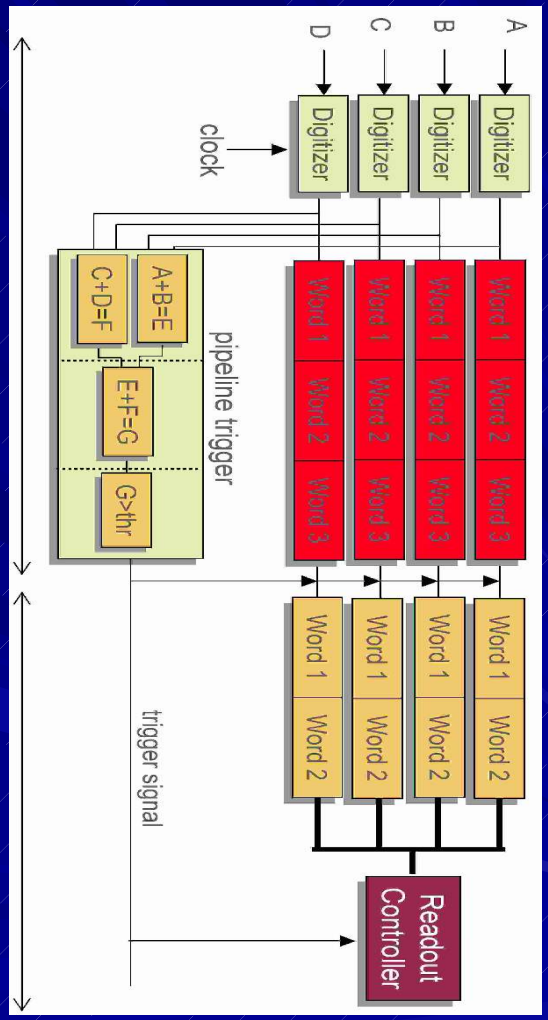


Digitisation

Pipeline

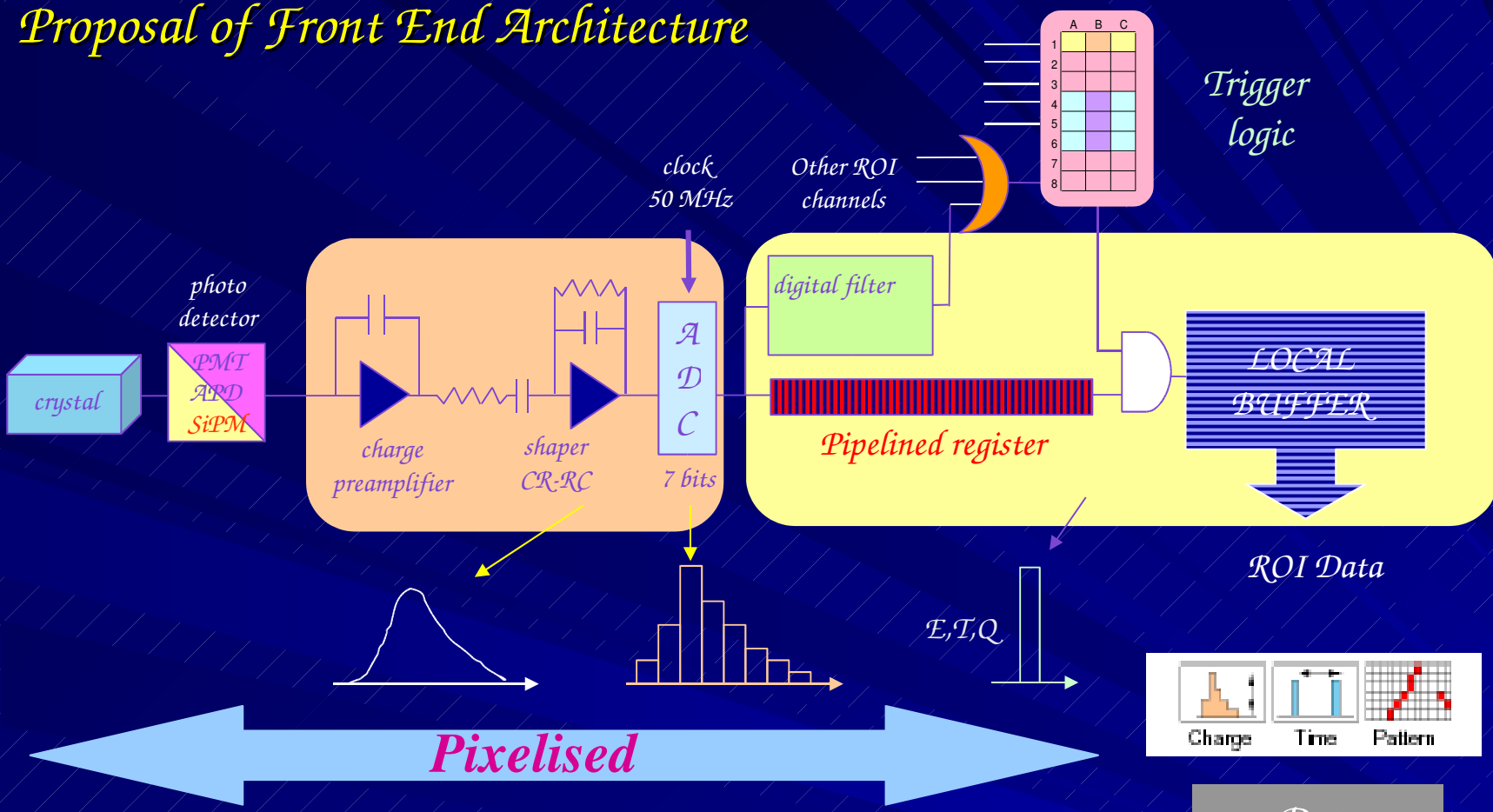
Event builder

Future PET



P. Le Du/Saclay

Proposal of Front End Architecture



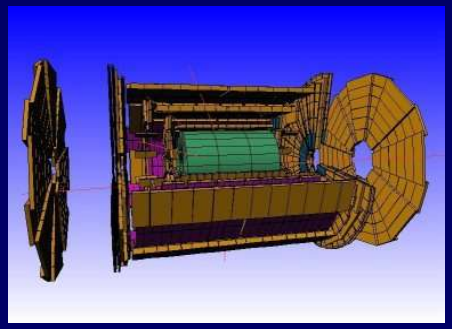
Pixelised

Data Acquisition

Trigger logic processes "raw fast information"
Free-running sampling ADC
Digital filter used to extract pulse amplitude and high resolution timing
Pipelined processing architecture to avoid deadtimes
Only one "channel" to compute either the energy and time

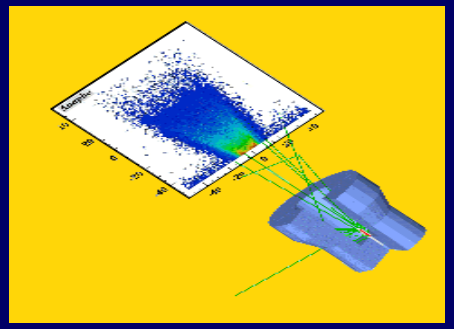
Geant4 – A Common Simulation Platform

High Energy Physics

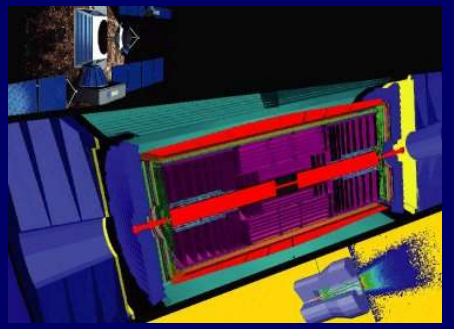


Space and Radiation

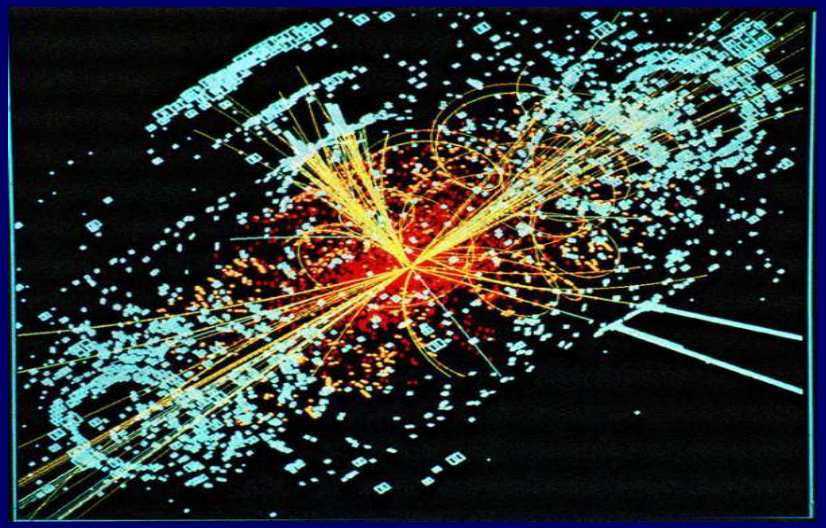
Medical



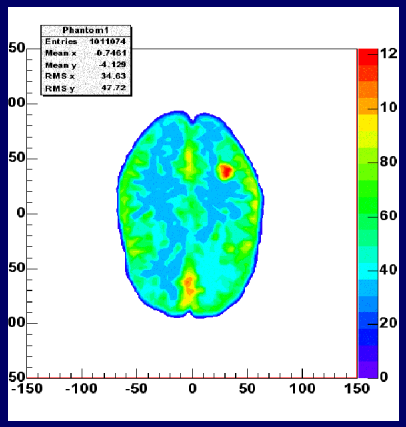
Technology Transfer

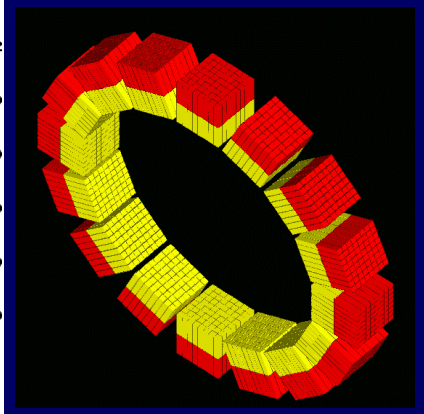


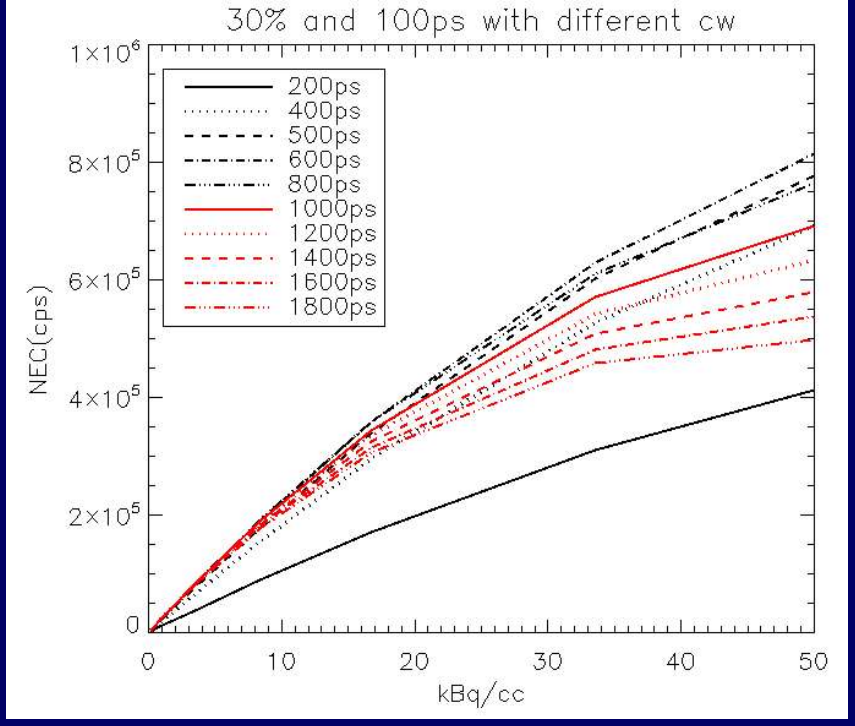
Higgs event at LHC (CMS) with Geant4

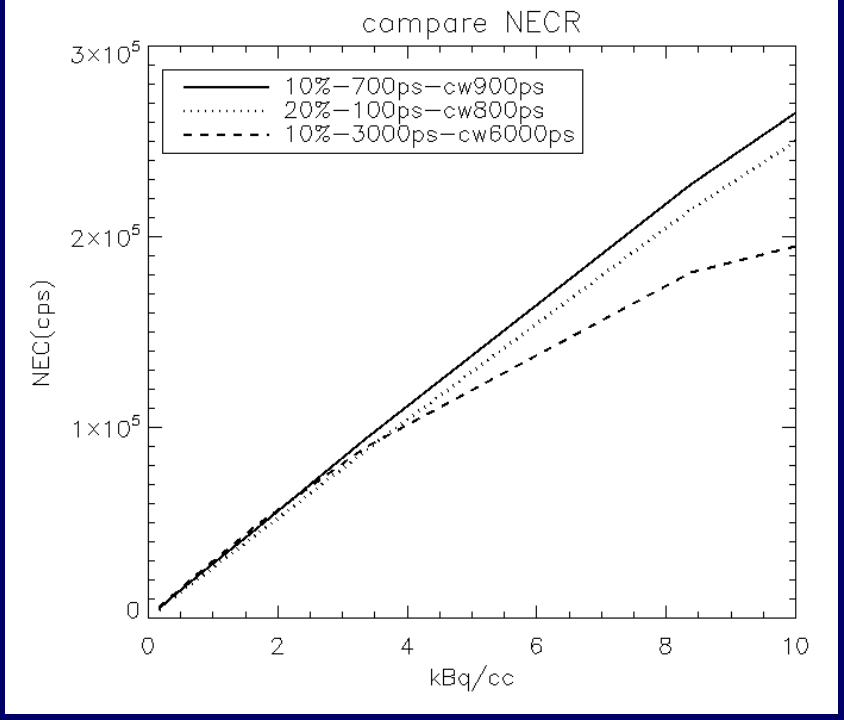


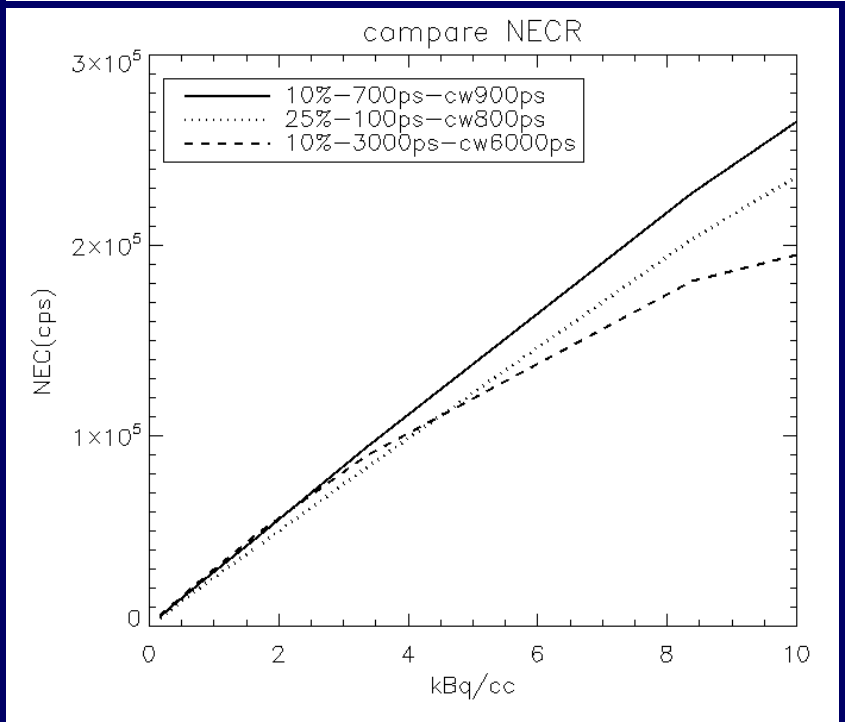
GATE -- Geant4 Application for Tomographic Emission

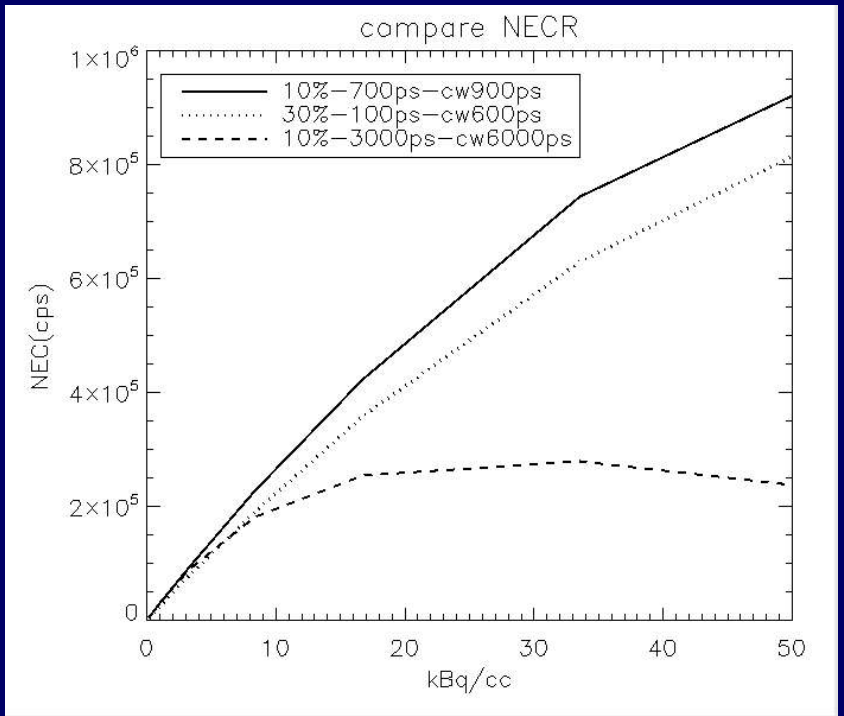





30% and 100ps with different cw
200ps
400ps
500ps
600ps
800ps
1000ps
1200ps
1400ps
1600ps
1800ps
NEC(cps)
kBq/cc

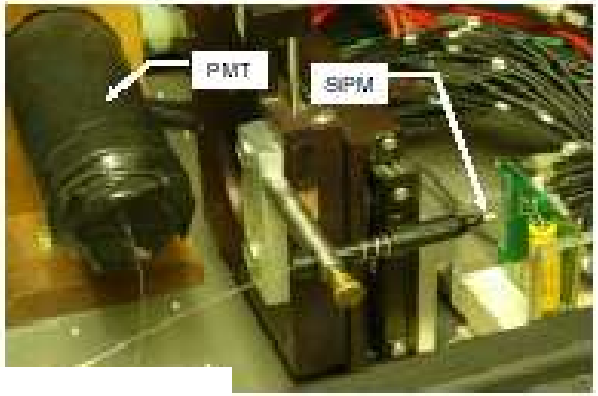

compare NECR
10%−700ps−cw900ps
20%−100ps−cw800ps
10%−3000ps−cw6000ps
NEC(cps)
kBq/cc

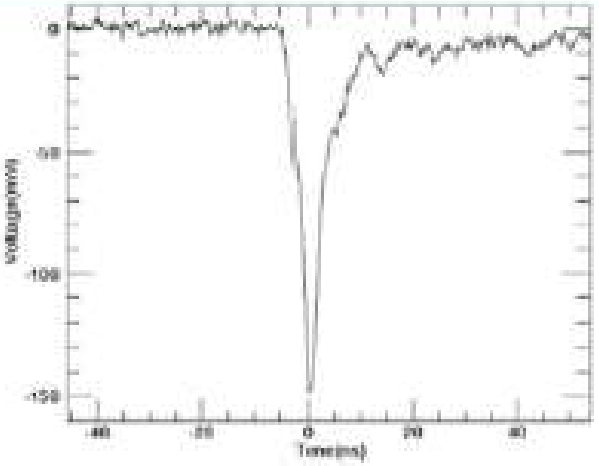

compare NECR
10%−700ps−cw900ps
25%−100ps−cw800ps
10%−3000ps−cw6000ps
NEC(cps)
kBq/cc

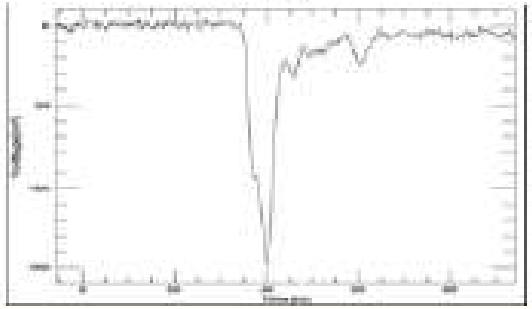

compare NECR
10%−700ps−cw900ps
30%−100ps−cw600ps
10%−3000ps−cw6000ps
NEC(cps)
kBq/cc

SiPM/PET Collaboration at ANL/UC

- Single photon response
- Pulsar-1156 SiPM in the test stand:







- Screen shots taken by Wagner and Xie:
  - No preamplifier