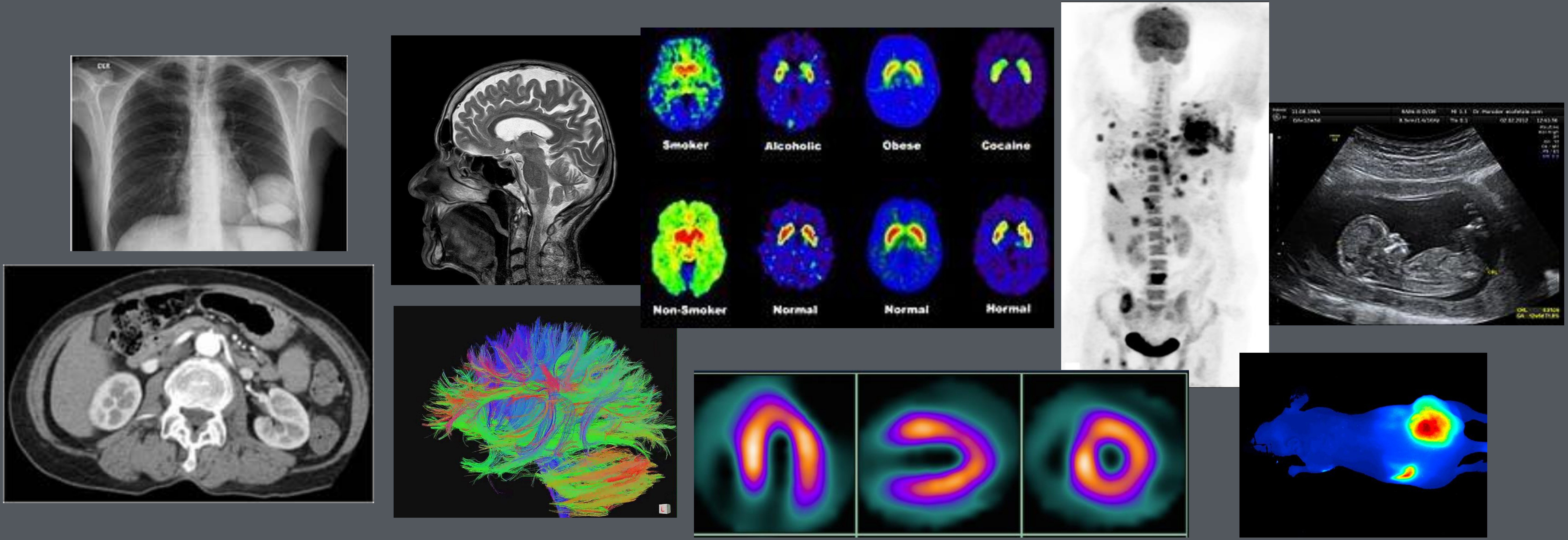
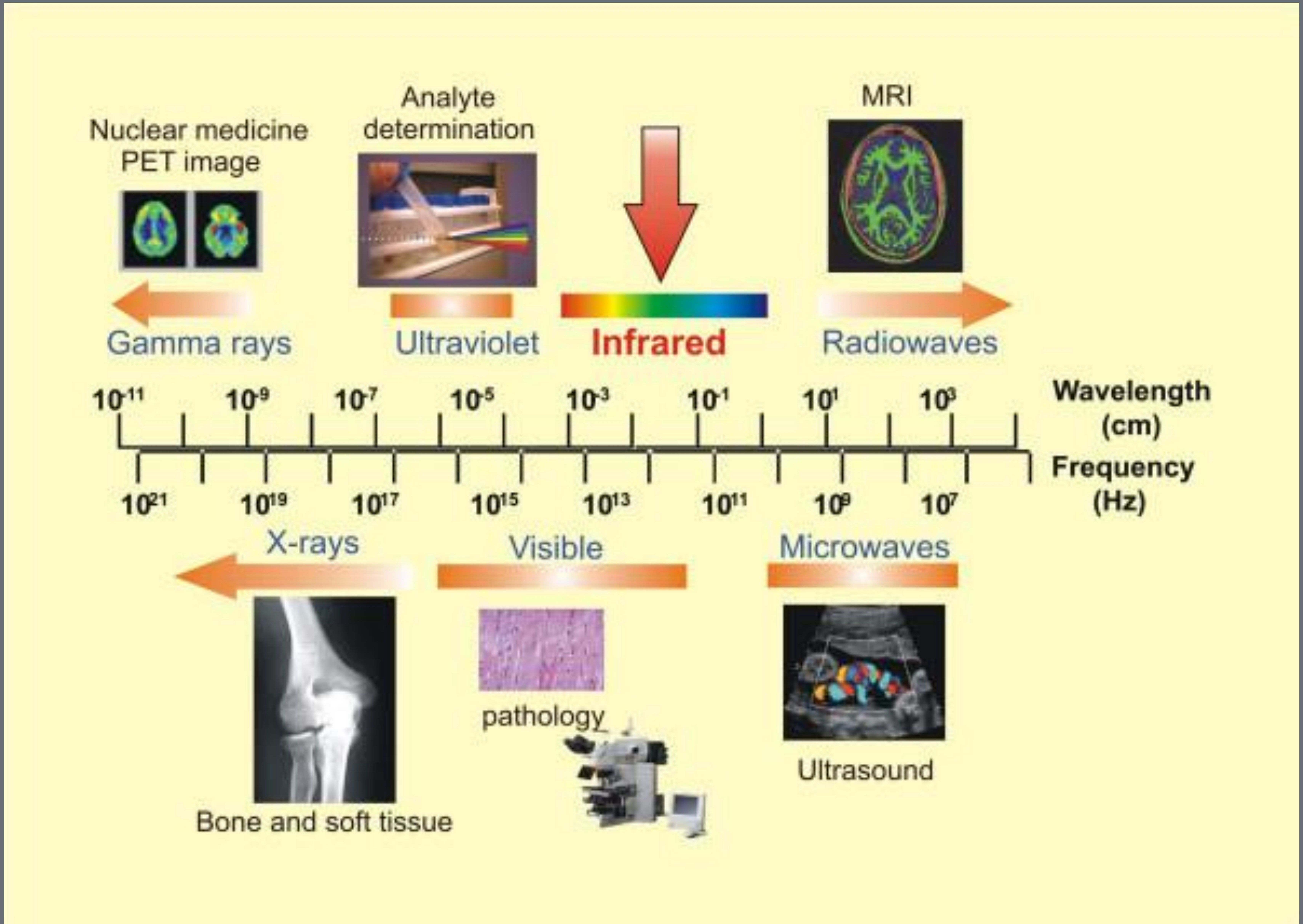
Medical Imaging

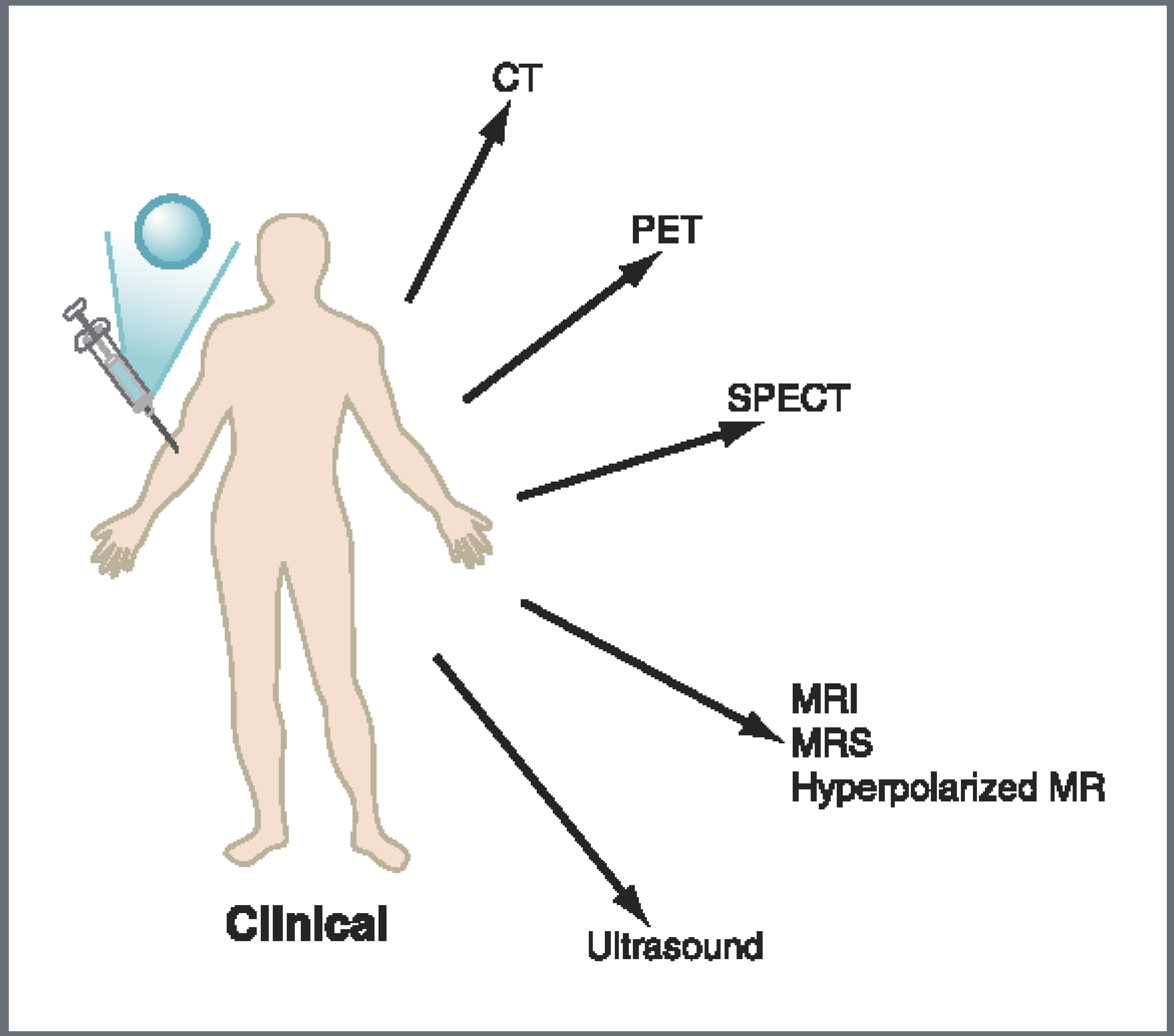


Chien-Min Kao
Associate Professor, Radiology and Medical Physics
University of Chicago

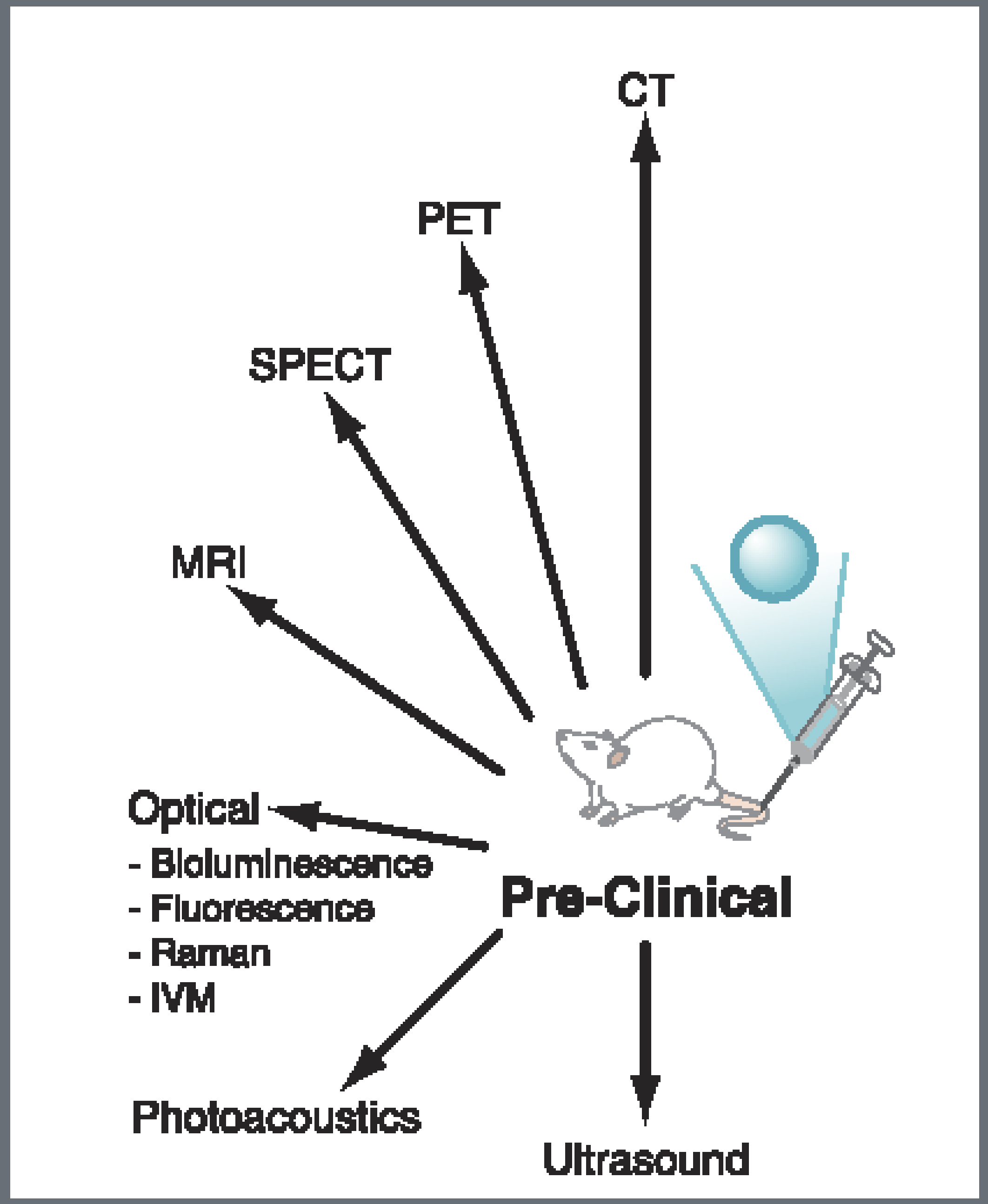
Excellent in Detector Instrumentation and Technology 2018, Fermi Lab, 3-14-2018



Nuclear medicine
PET image
Analyte
determination
MRI
Gamma rays
Ultraviolet
Infrared
Radiowaves
10^{-11} 10^{-9} 10^{-7} 10^{-5} 10^{-3} 10^{-1} 10^{1} 10^{3}
Wavelength
(cm)
Frequency
(Hz)
10^{21} 10^{19} 10^{17} 10^{15} 10^{13} 10^{11} 10^{9} 10^{7}
X-rays
Visible
Microwaves
pathology
Ultrasound
Bone and soft tissue

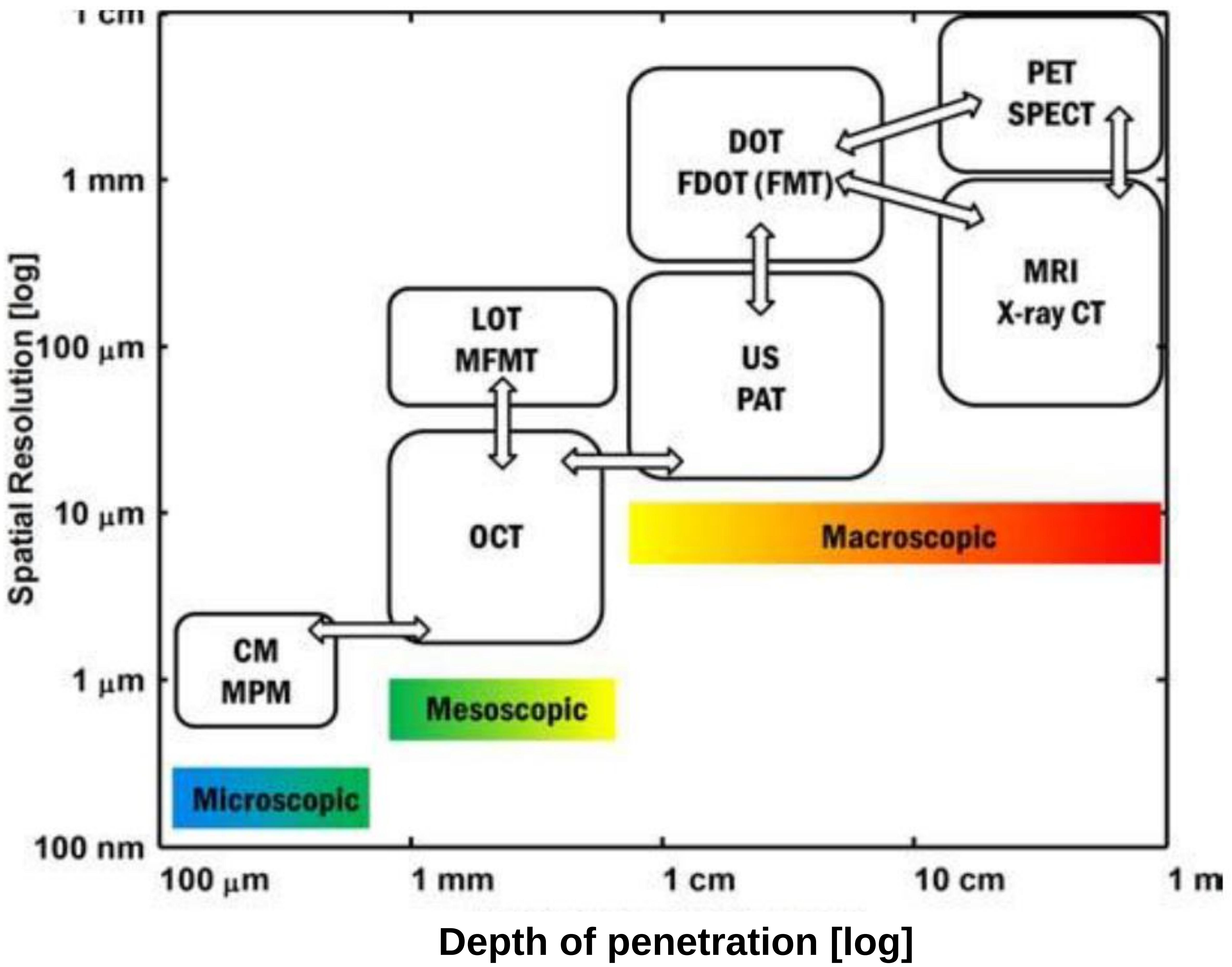


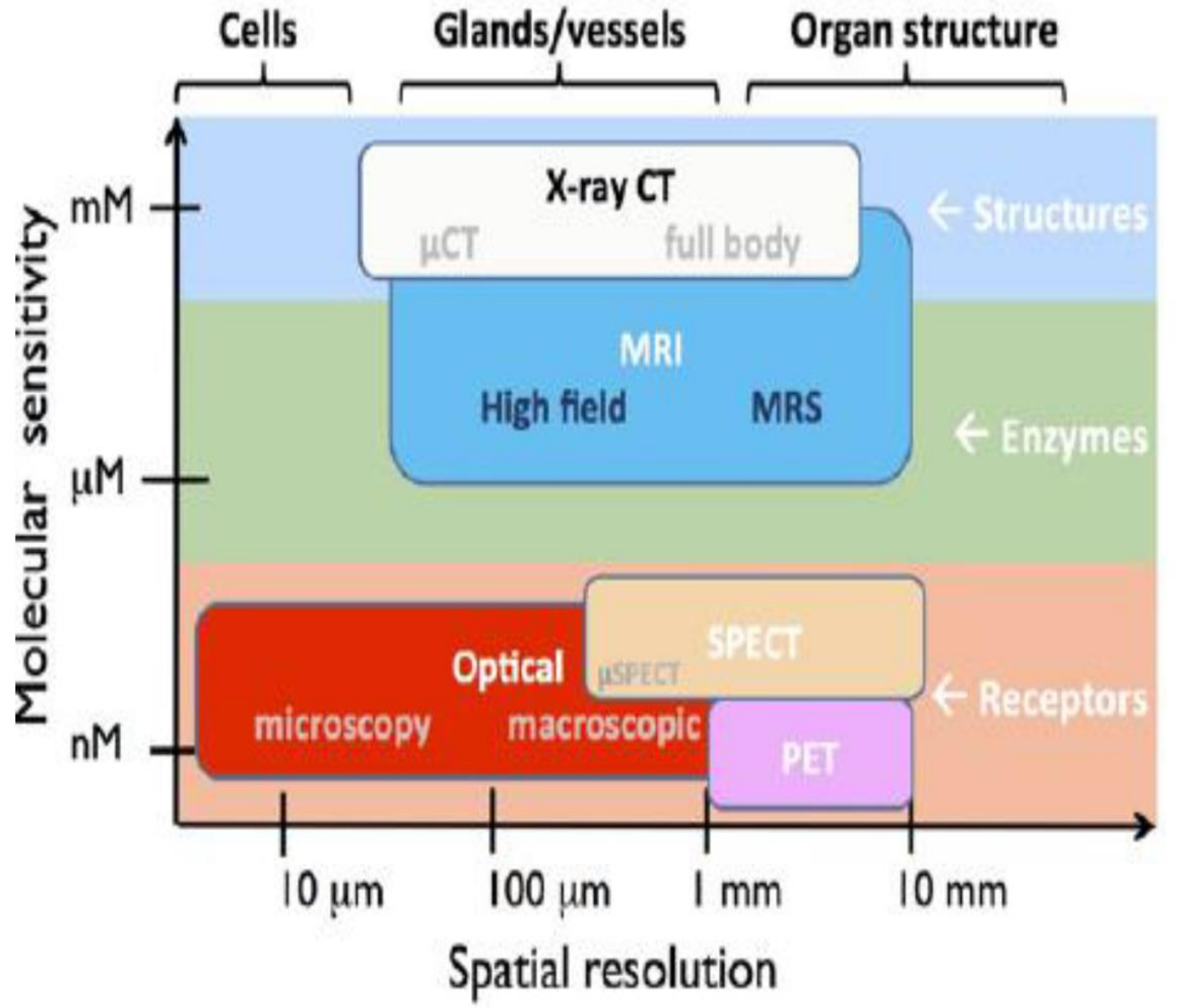
CT
PET
SPECT
MRI
MRS
Hyperpolarized MR
Clinical
Ultrasound

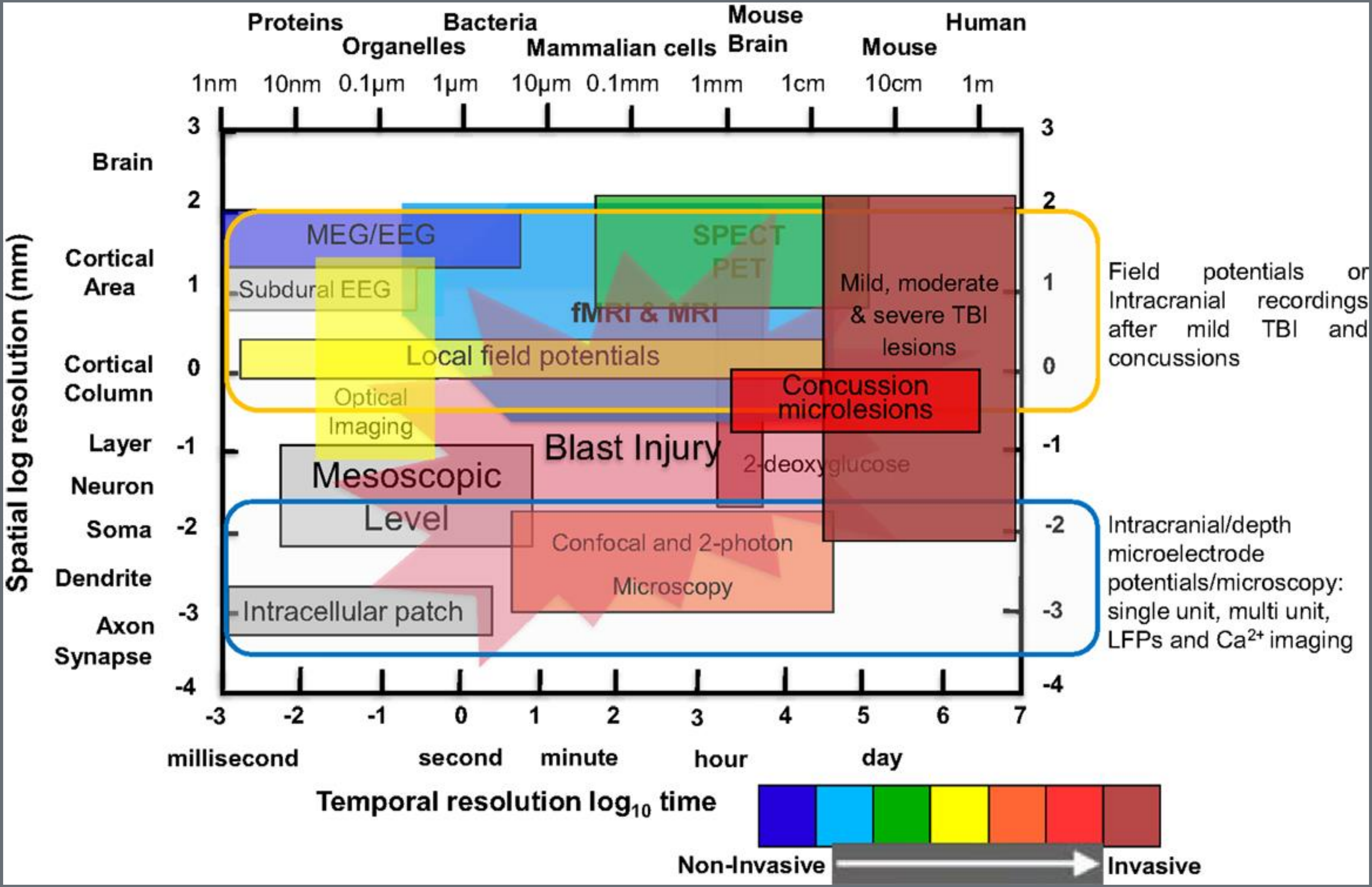


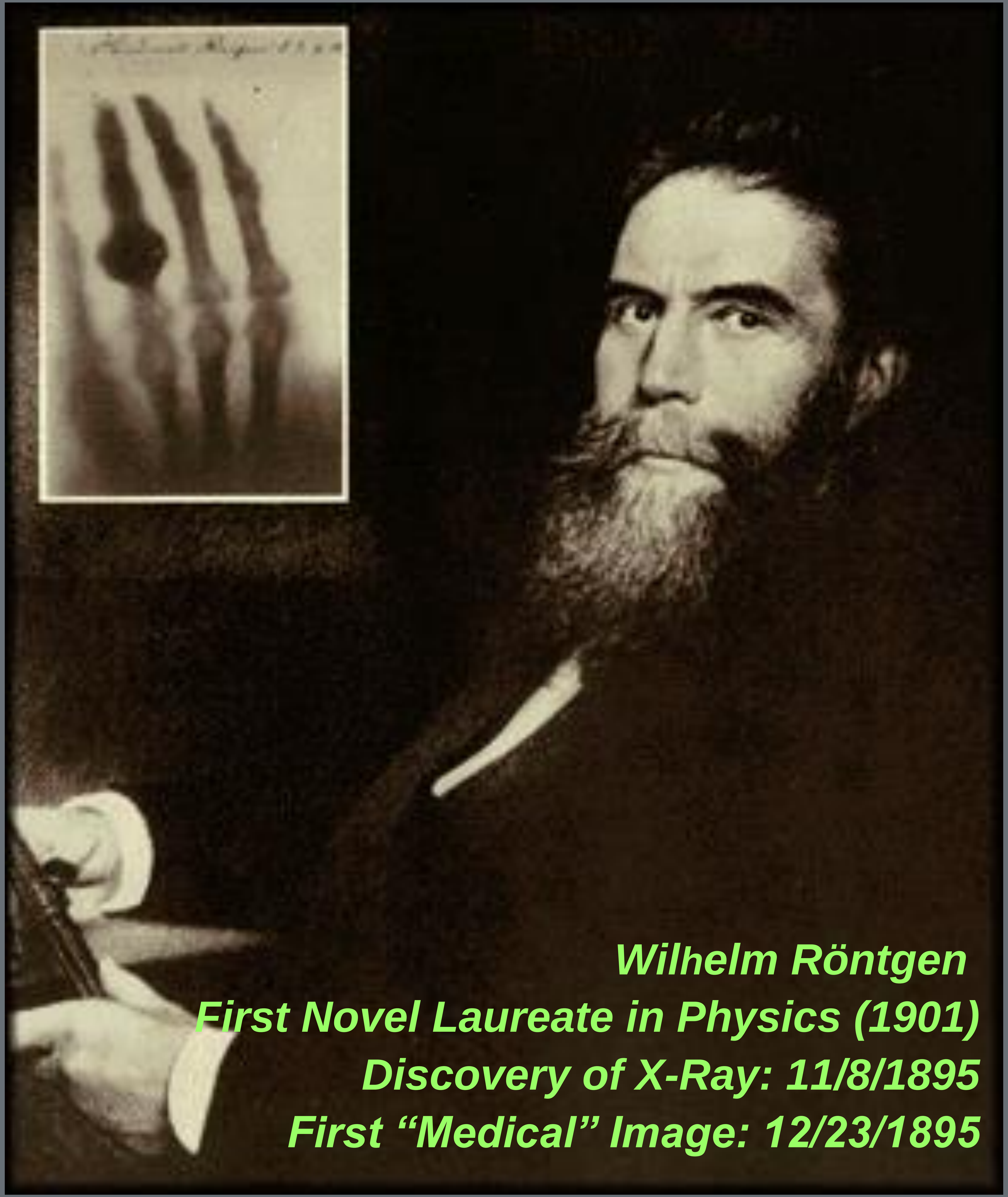
CT
PET
SPECT
MRI
Optical
- Bioluminescence
- Fluorescence
- Raman
- IVM
Pre-Clinical
Photoacoustics
Ultrasound

CM: confocal microscopy; MPM: multi-photon microscopy; LOT: laminar optical tomography; (M)FMT: (mesoscopic) Fluorescence molecular tomography; OCT: optical coherent tomography; (M)DOT: (mesoscopic) diffuse optical tomography; PAT: photoacoustic tomography

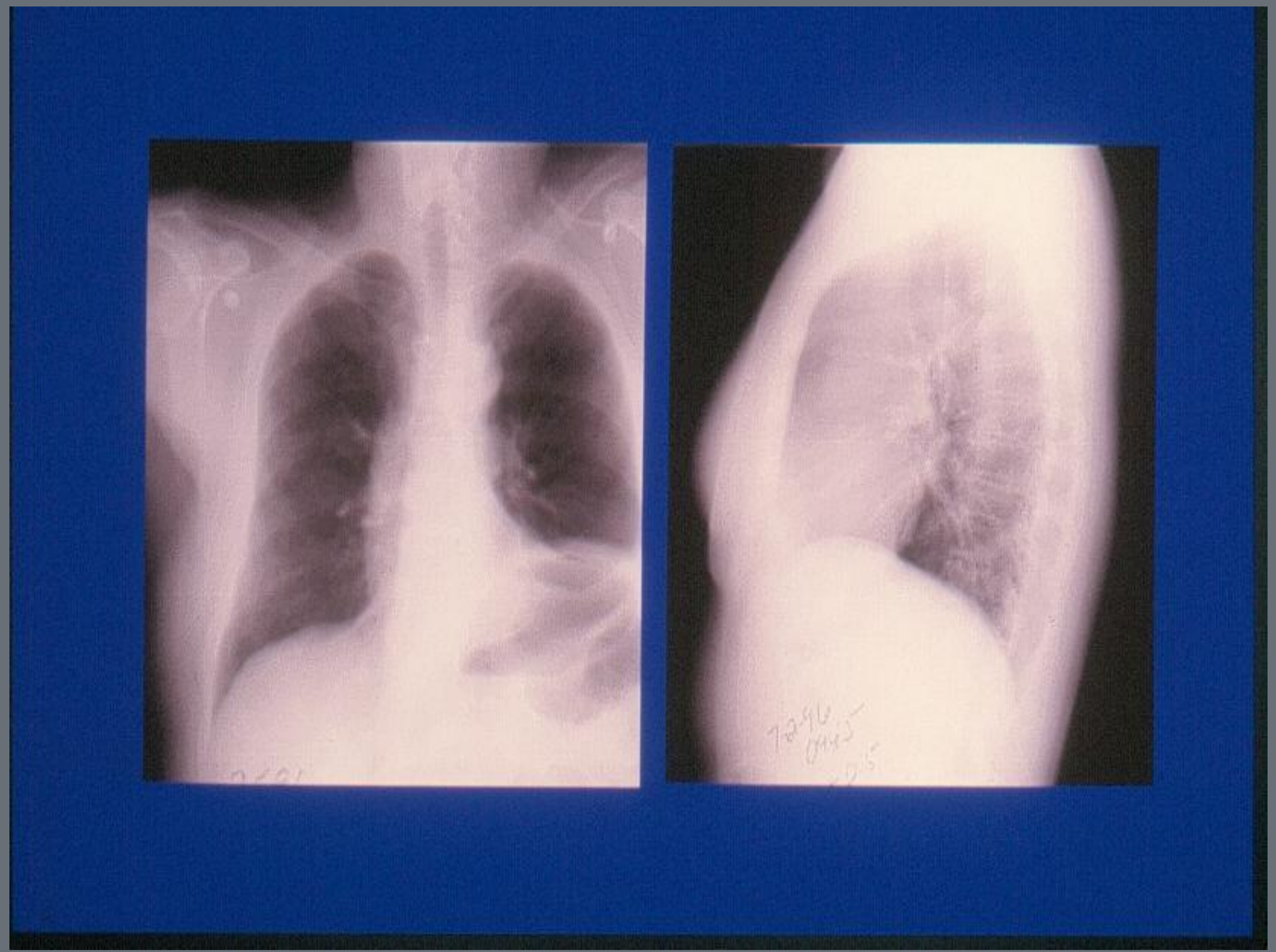





Proteins
Organelles
Bacteria
Mammalian cells
Mouse Brain
Mouse
Human
1nm 10nm 0.1µm 1µm 10µm 0.1mm 1mm 1cm 10cm 1m
Spatial log resolution (mm)
Brain
Cortical Area
Cortical Column
Layer
Neuron
Soma
Dendrite
Axon
Synapse
3 2 1 0 -1 -2 -3 -4
MEG/EEG
Subdural EEG
SPECT
PET
fMRI & MRI
Mild, moderate & severe TBI lesions
Local field potentials
Optical Imaging
Concussion microlesions
Blast Injury
2-deoxyglucose
Mesoscopic Level
Confocal and 2-photon Microscopy
Intracellular patch
Field potentials or Intracranial recordings after mild TBI and concussions
Intracranial/depth microelectrode potentials/microscopy: single unit, multi unit, LFPs and Ca2+ imaging
-3 -2 -1 0 1 2 3 4 5 6 7
millisecond
second
minute
hour
day
Temporal resolution log10 time
Non-Invasive
Invasive

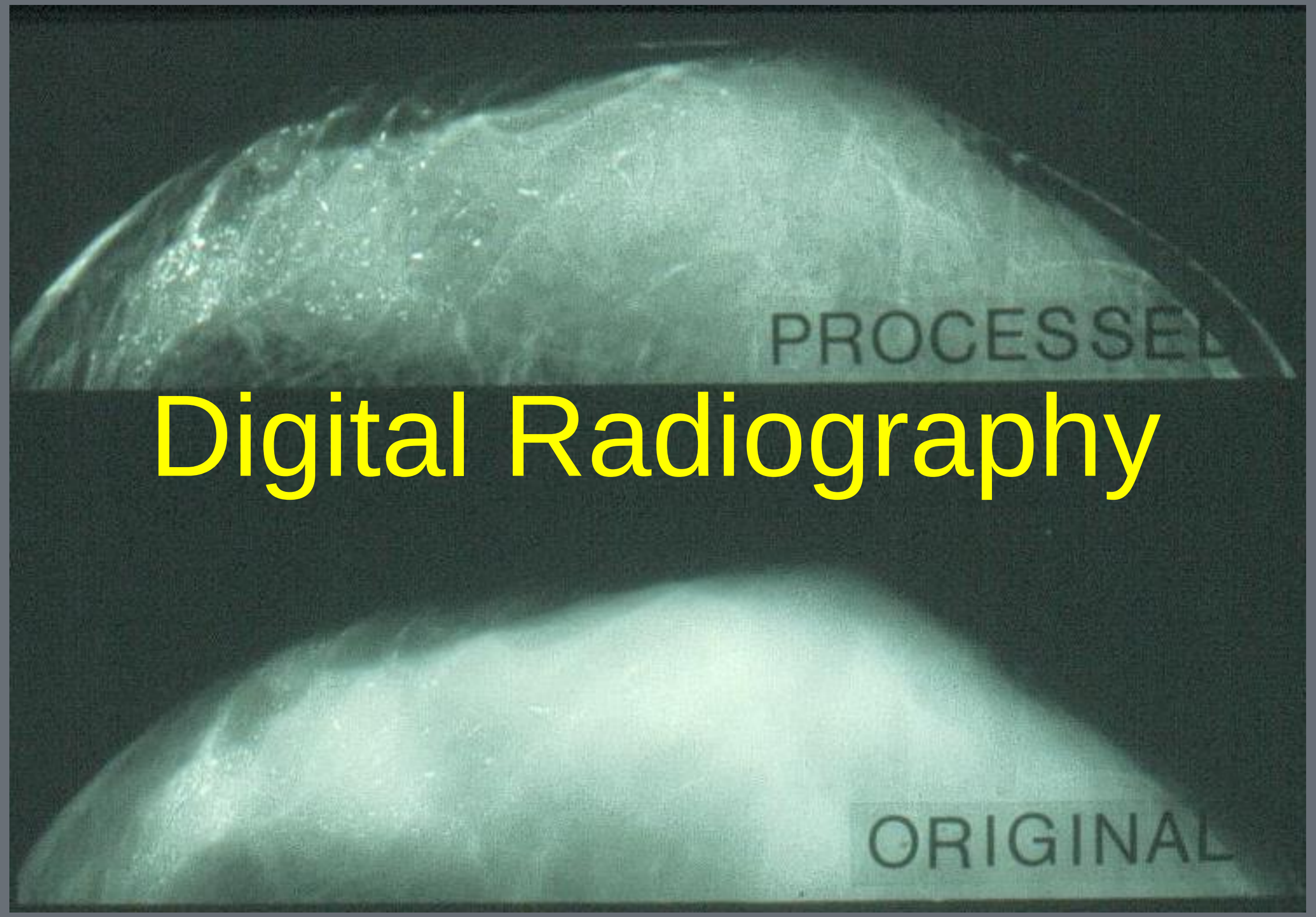


Wilhelm Röntgen
First Novel Laureate in Physics (1901)
Discovery of X-Ray: 11/8/1895
First “Medical” Image: 12/23/1895

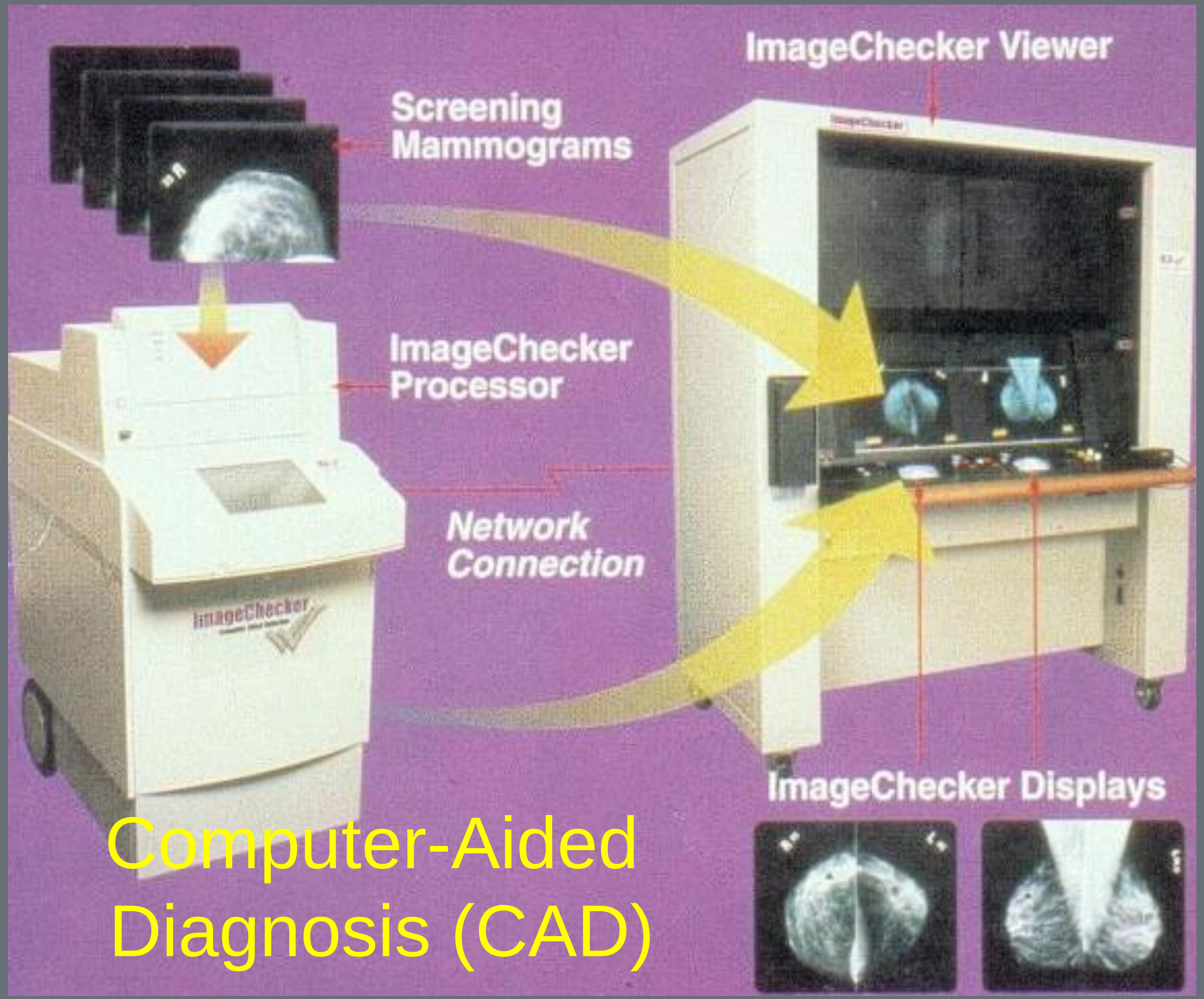


Anatomy Structure
3D→2D
Radiation

X-ray (~100keV)
Tissue Attenuation
Coefficient
(Electron Density)



Digital Radiography



Computer-Aided Diagnosis (CAD)

X-Ray Computed Tomography (CT)

X-ray (~100keV)

Tissue Attenuation Coefficient (Electron Density)

Anatomy & Structure

~1975

2001

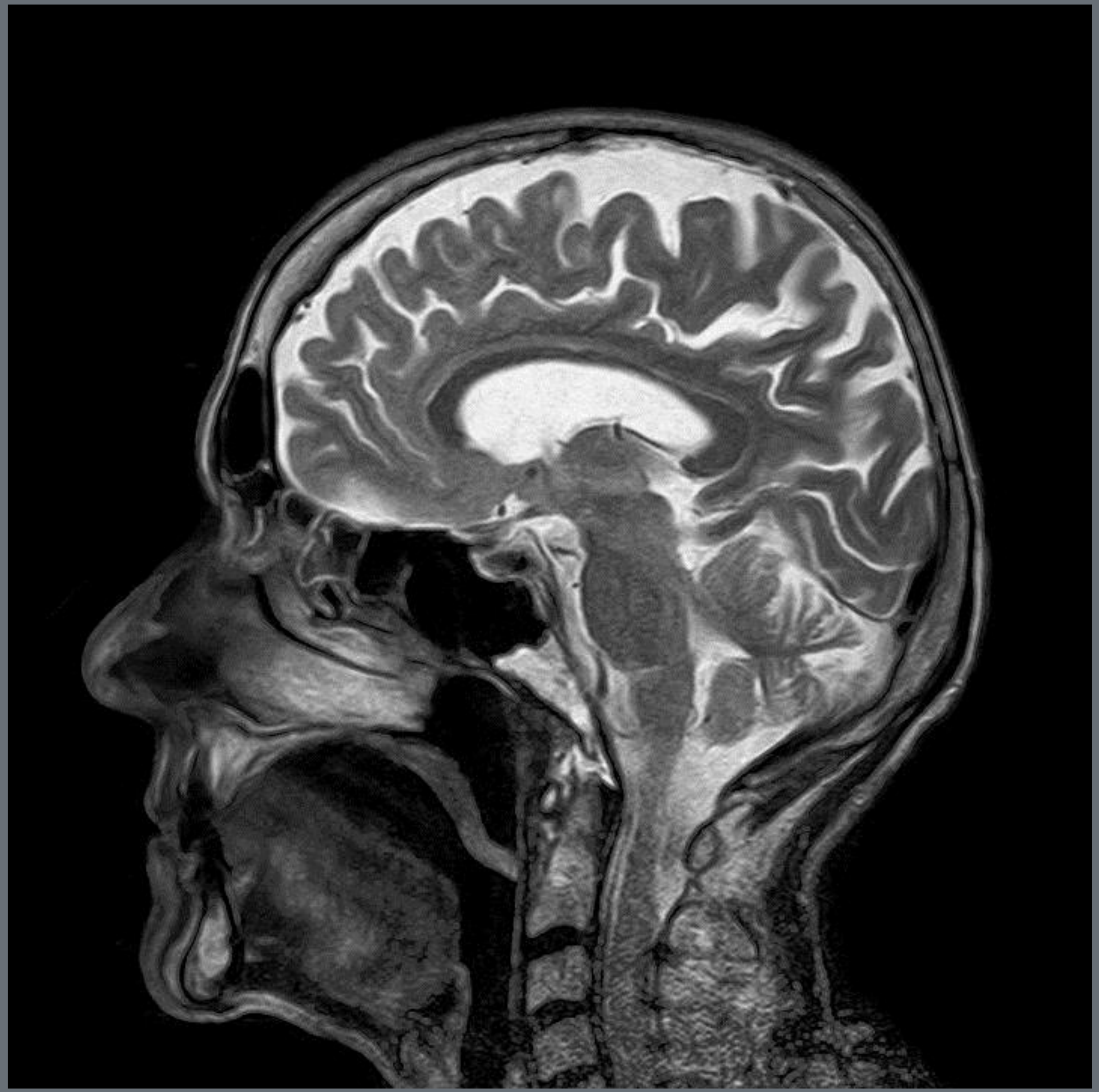
Alan M. Cormack
(1924-1998)

Sir Godfrey N. Hounsfield
(1919-2004)

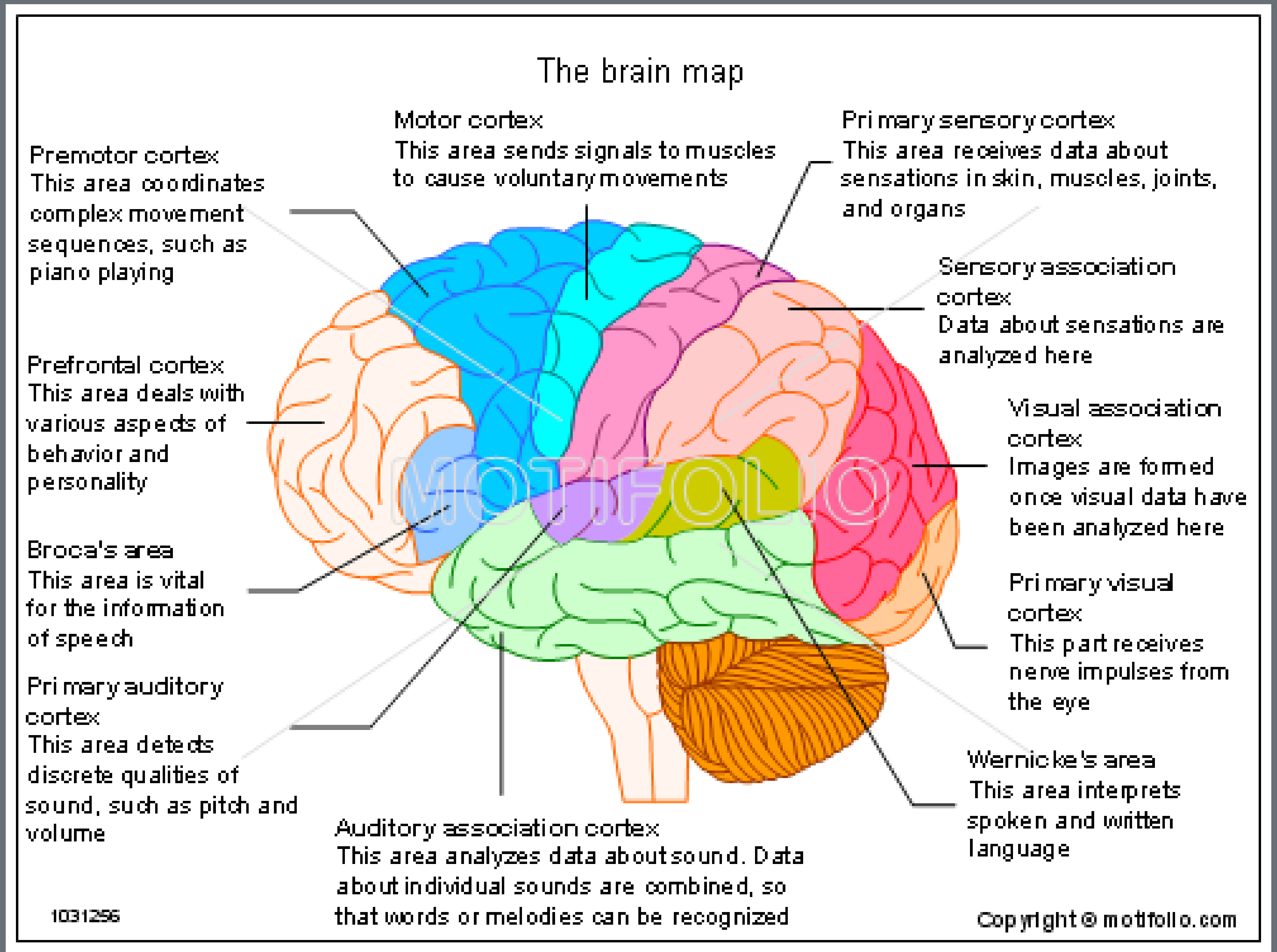
Medical CT spatial resolution: < 1 mm
Micro CT spatial resolution: ~ 1-10 mm

Alan M. Cormack and Sir Godfrey N. Hounsfield received the 1979 Nobel Prize in Physiology or Medicine for the development of computer assisted tomography (CT)

Functional vs Anatomical Imaging

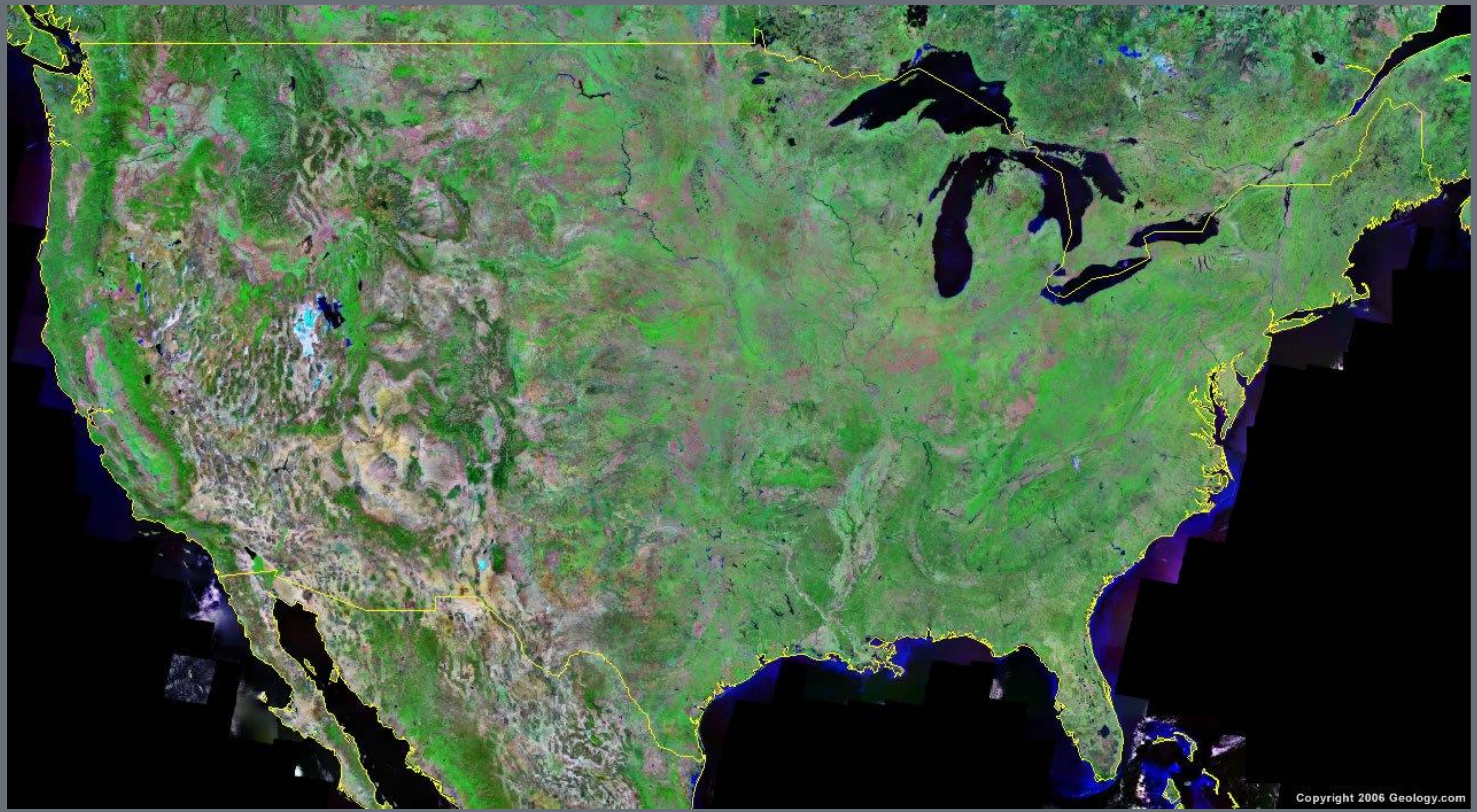


Live or dead brain?



Functional imaging

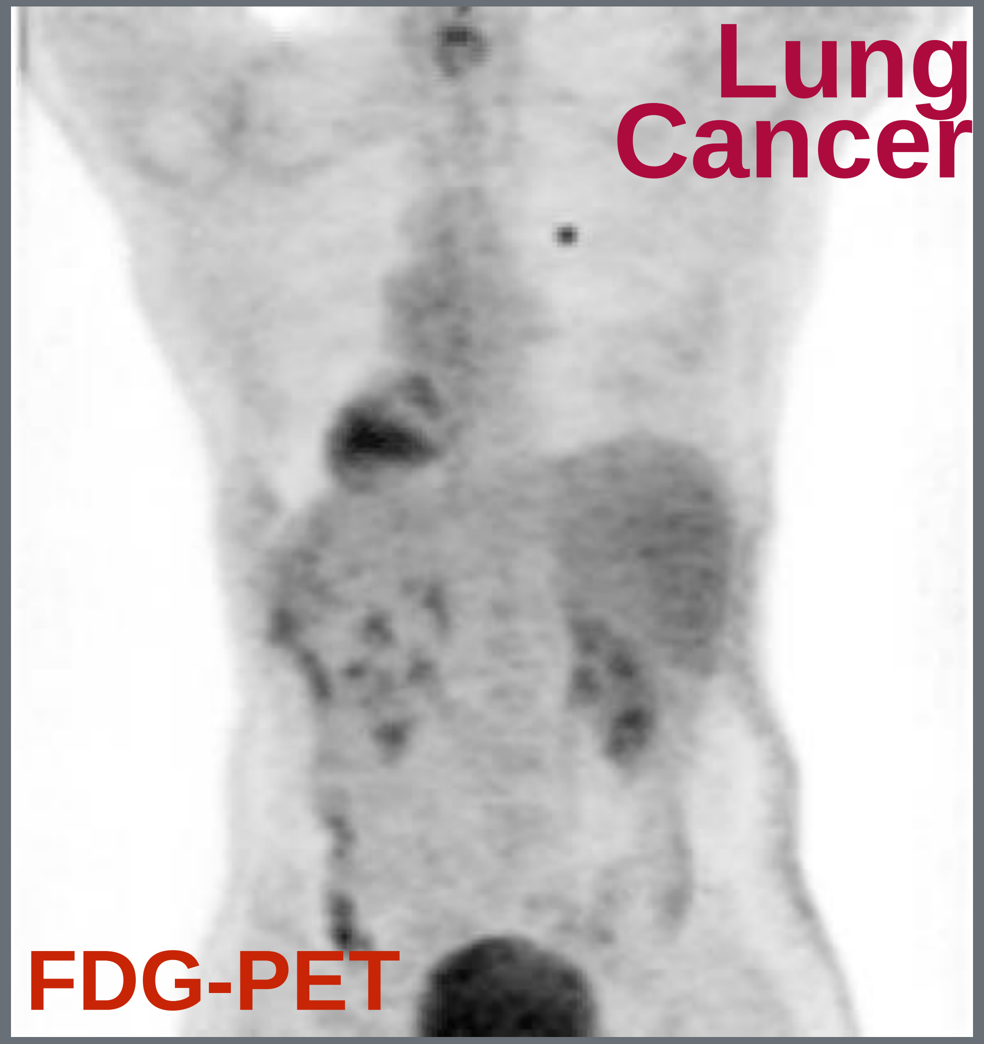
“light up” activities

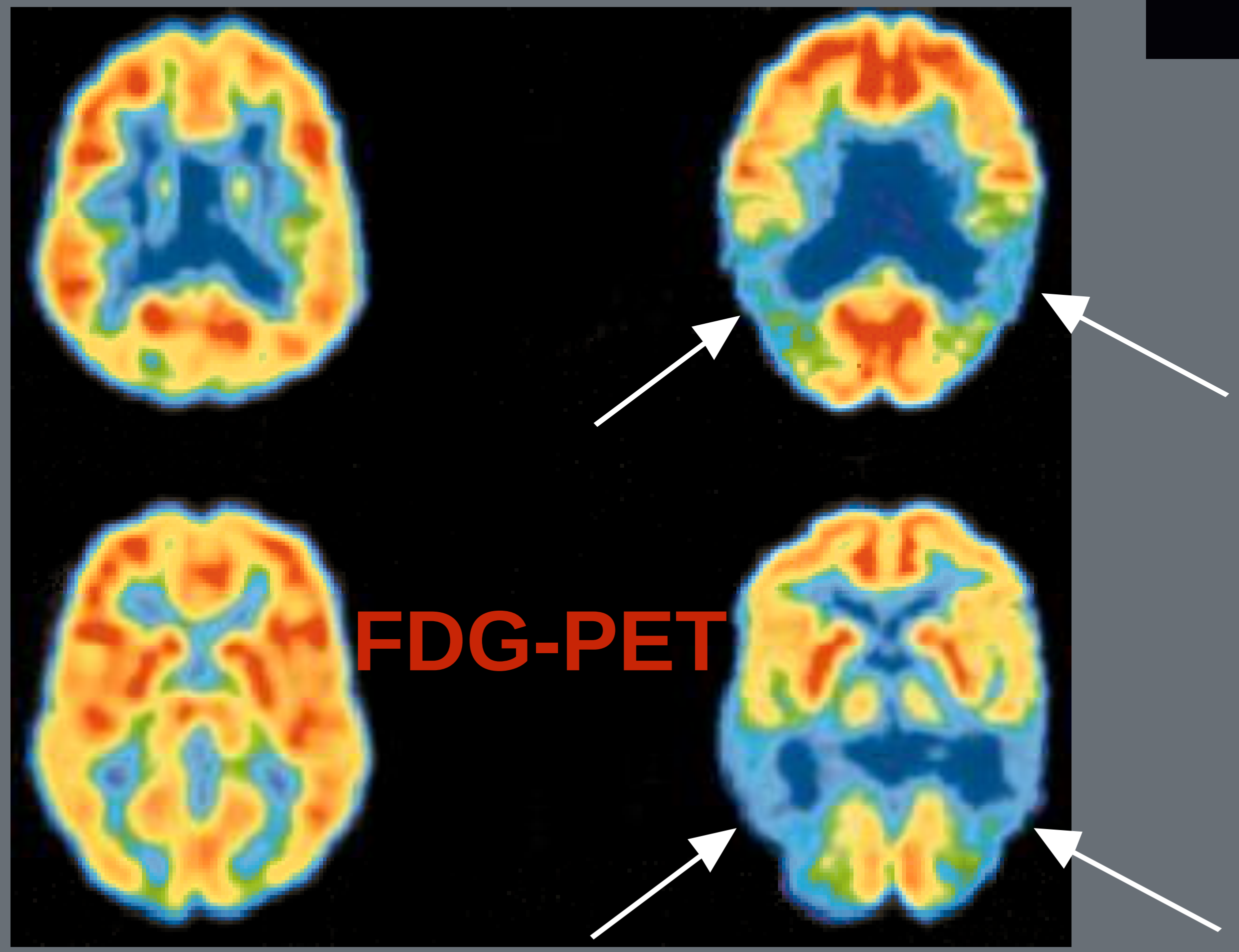


Nuclear Medicine Imaging

Tracer Kinetics & Distribution
+ Radiolabeled chemicals
= Function/Physiology

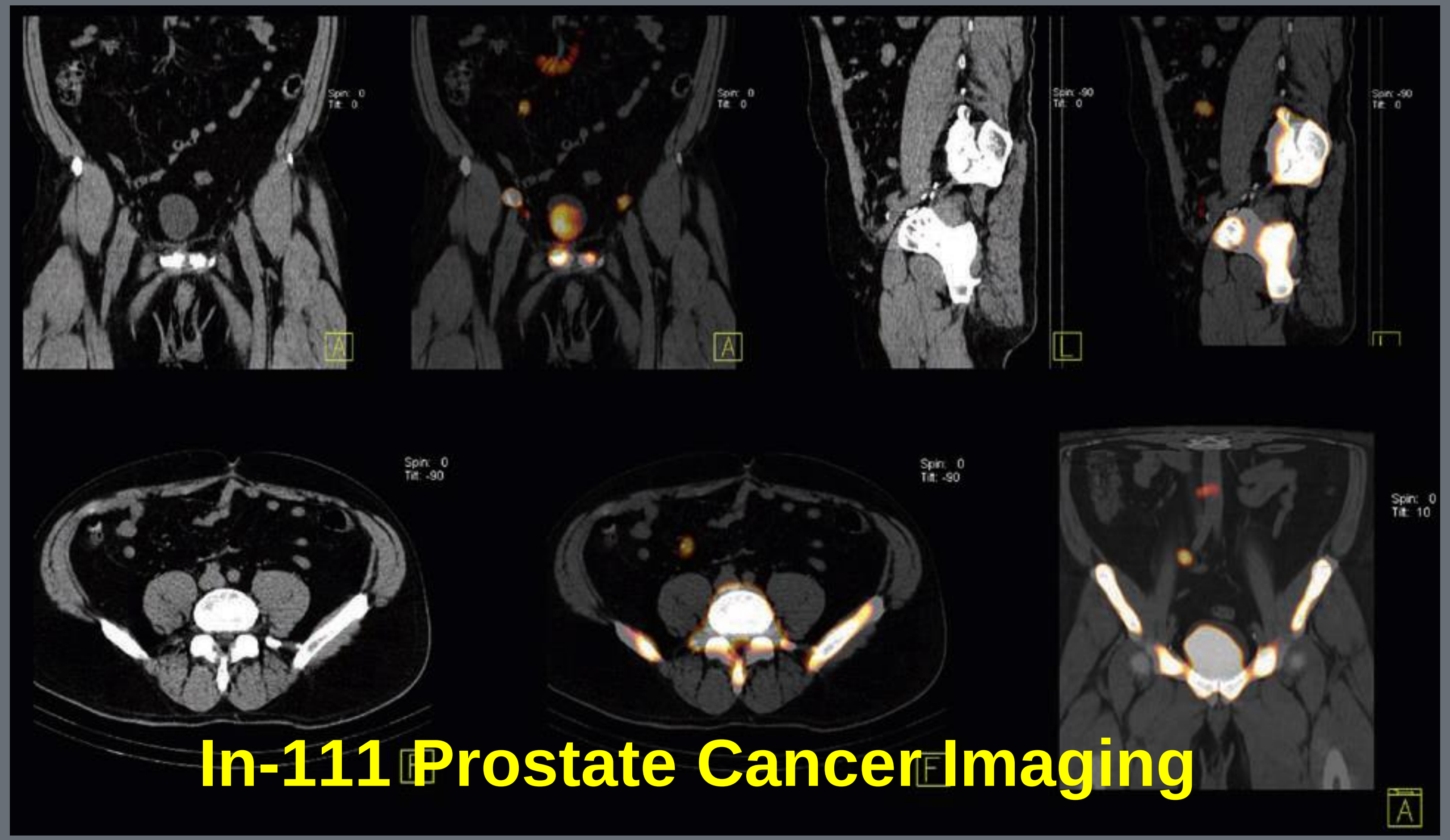
➔ molecular imaging



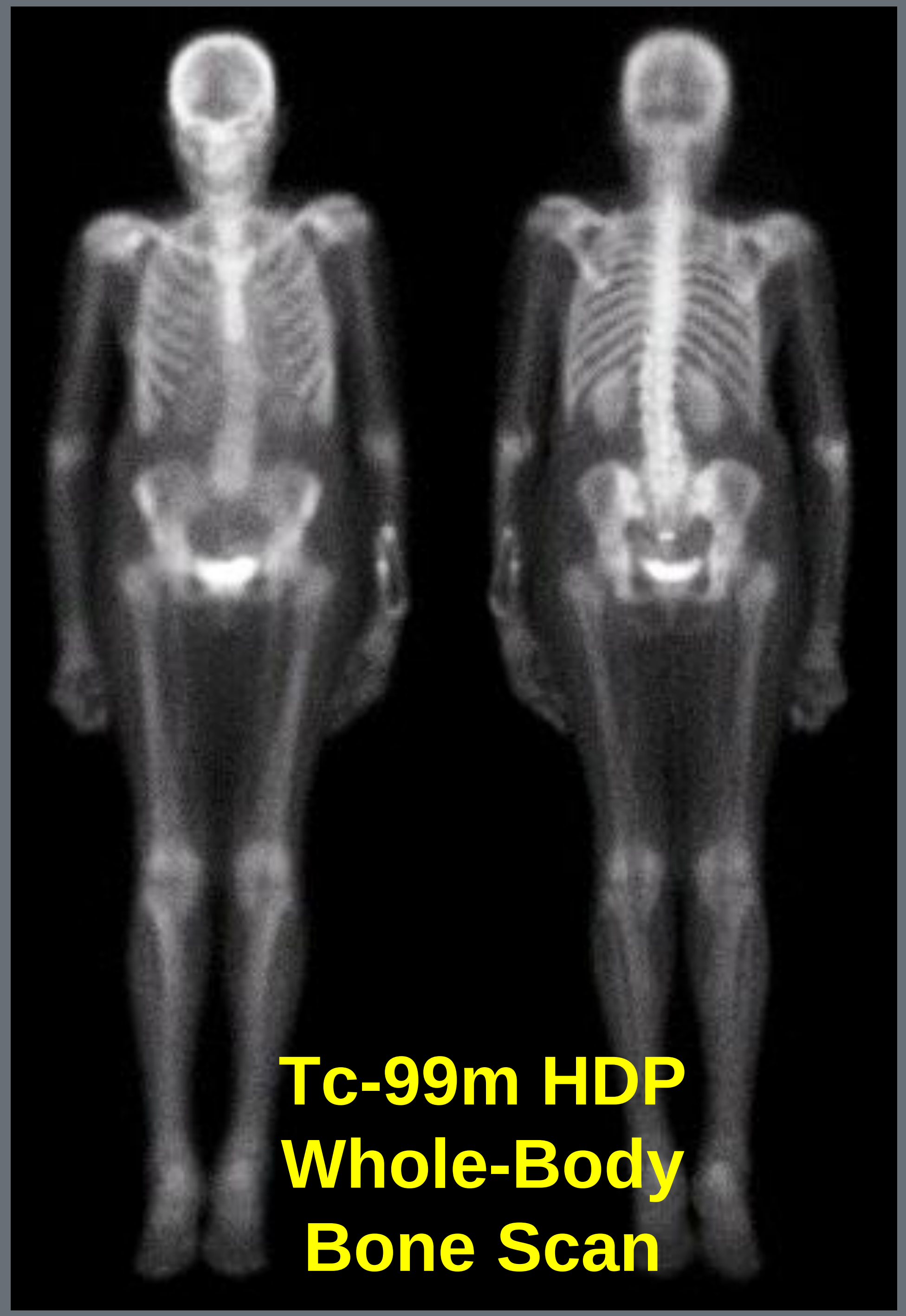


Normal

Alzheimer's Disease

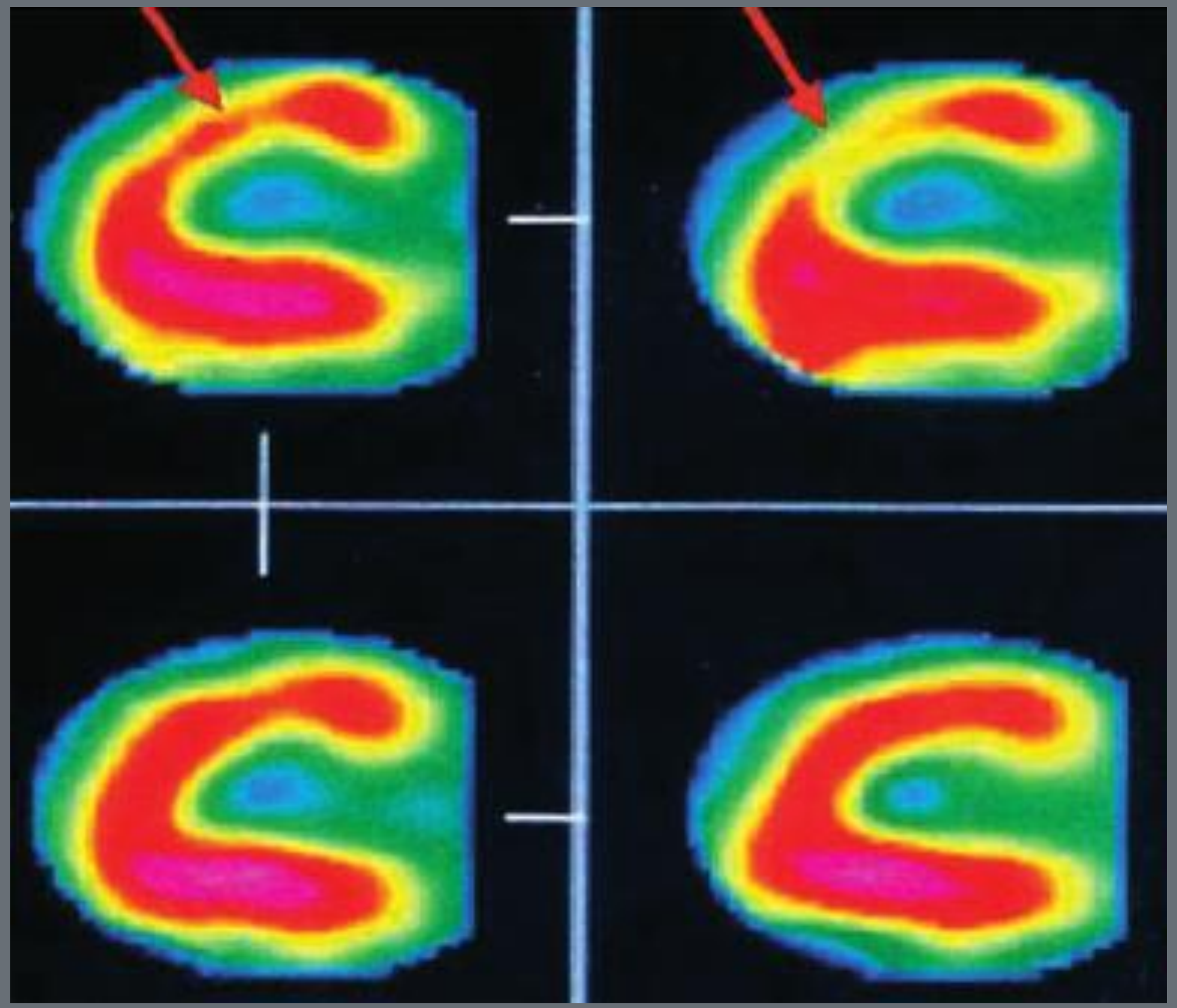


Planar & Single-Photon ECT (SPECT))

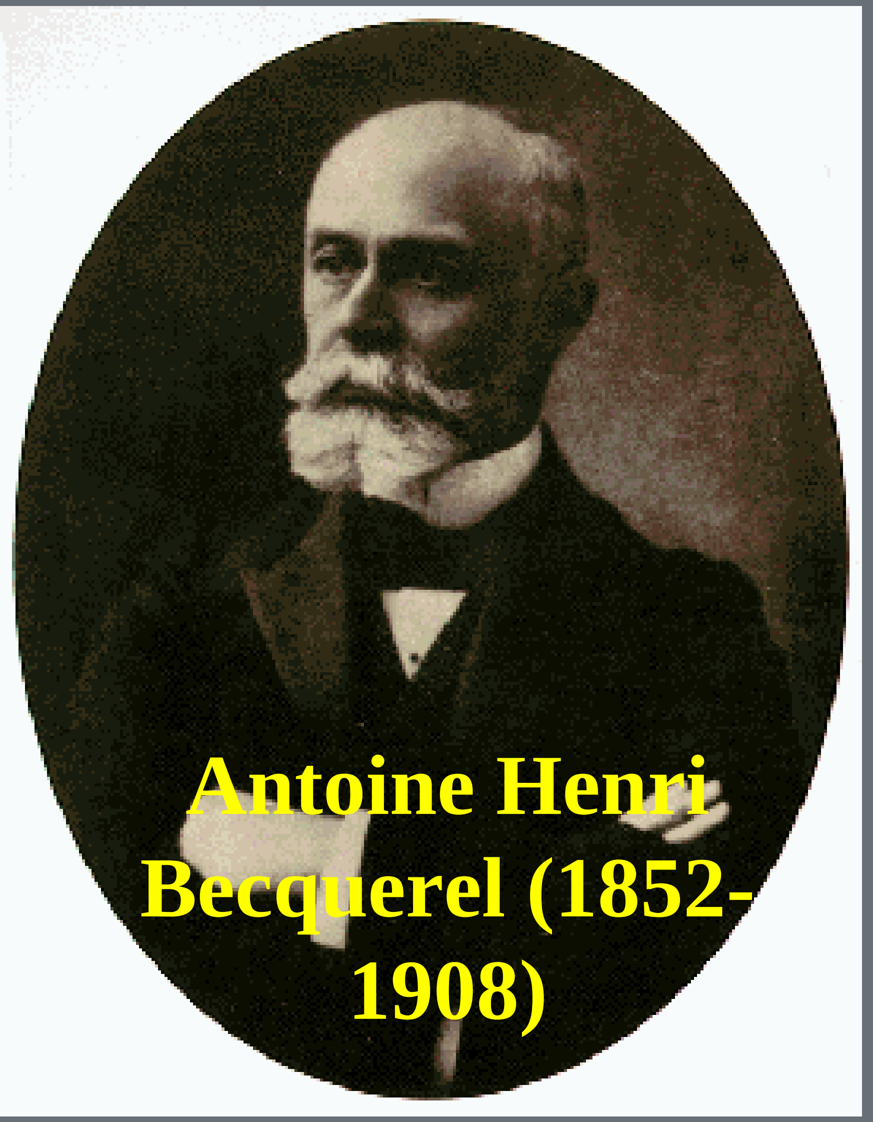


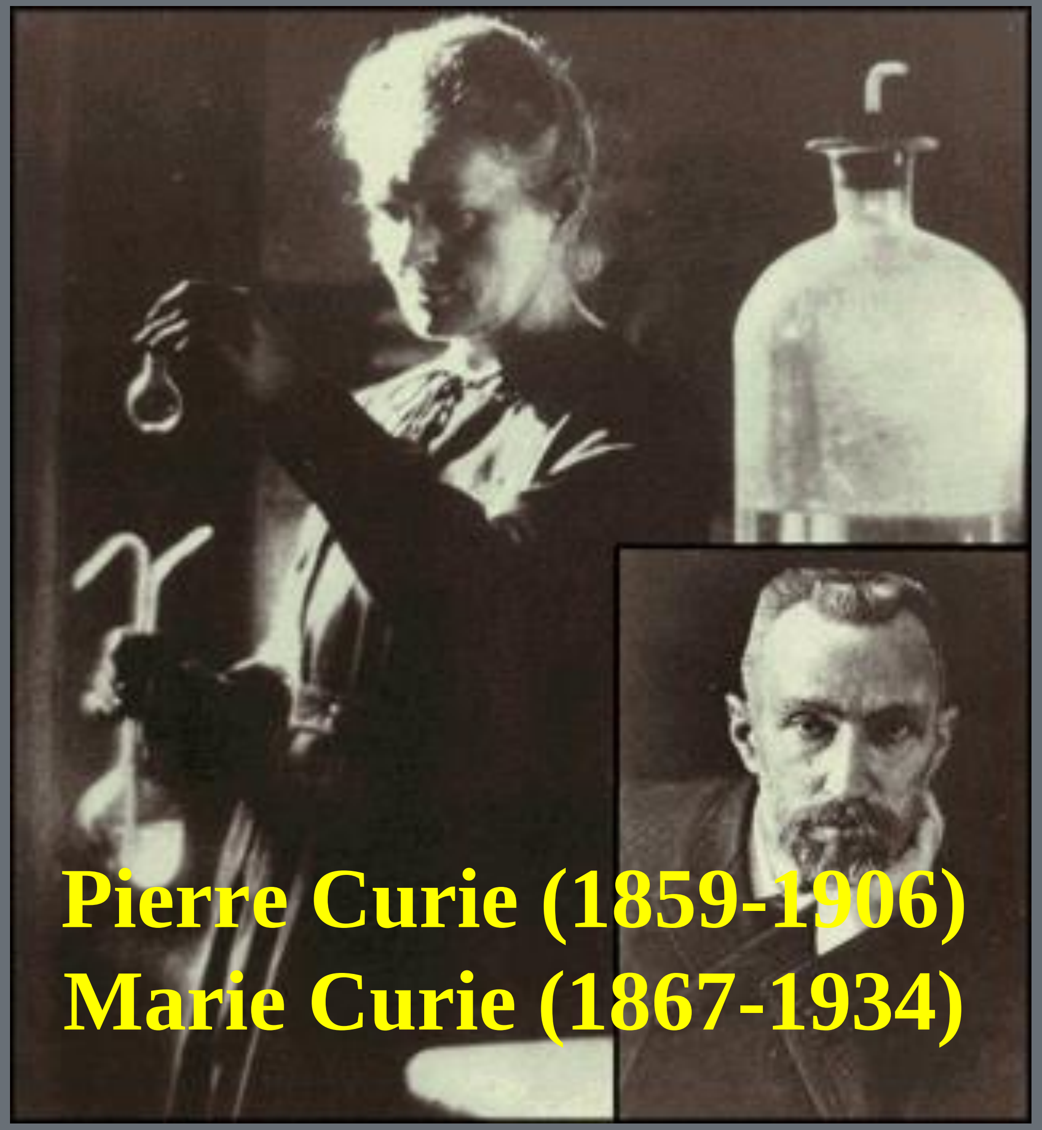
stress

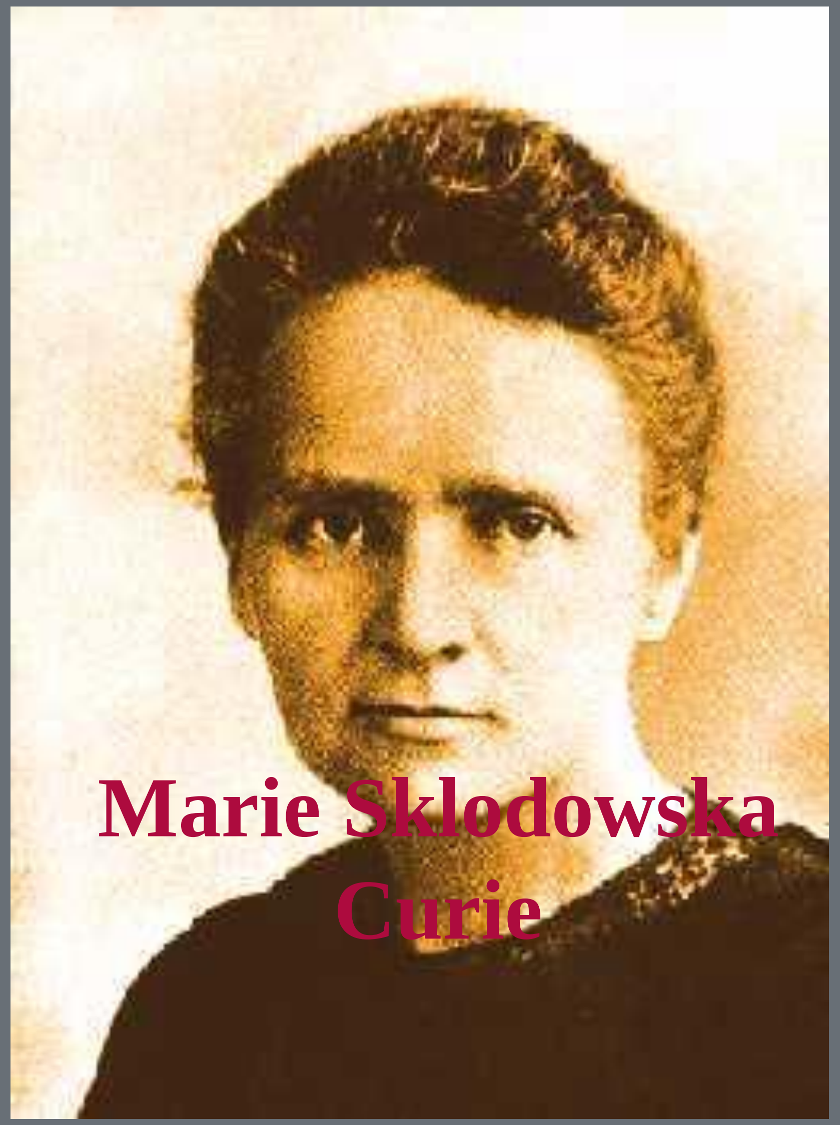
rest

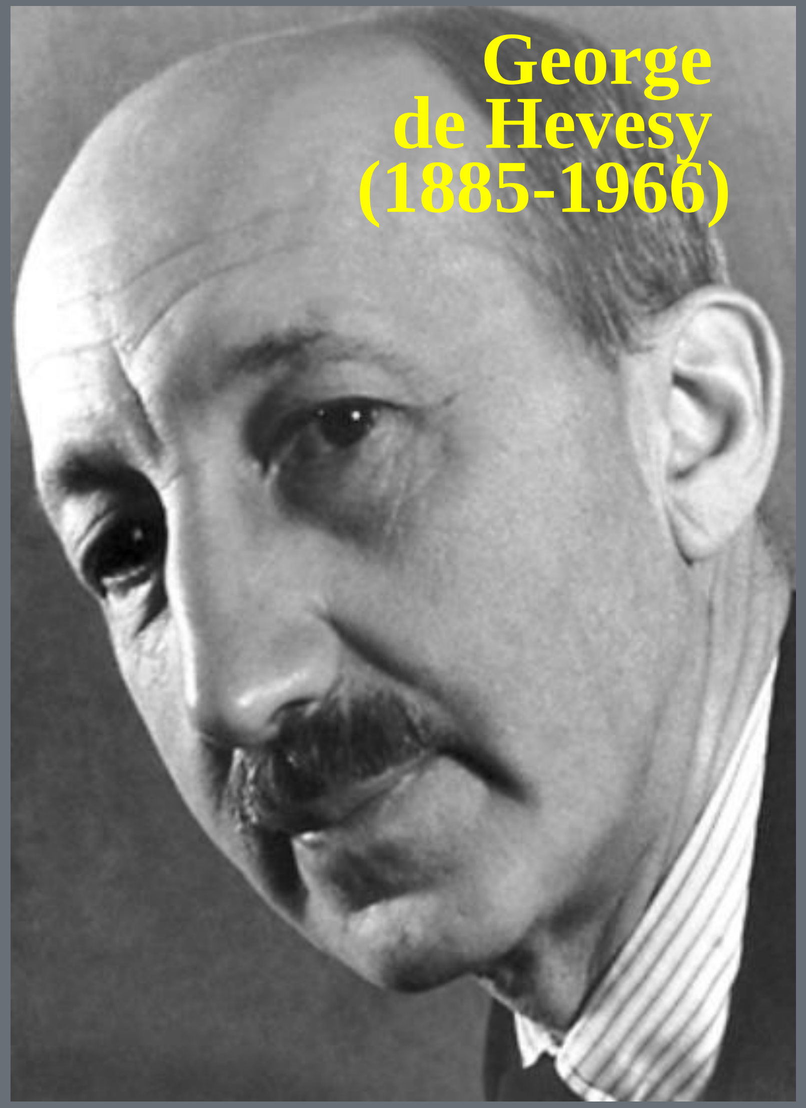


Tl-201 Cardiac Functional Scan









Nobel Prize in Physics, 1903: Antoine Henri Becquerel, Pierre Curie, Marie Curie for the discovery of spontaneous radioactivity

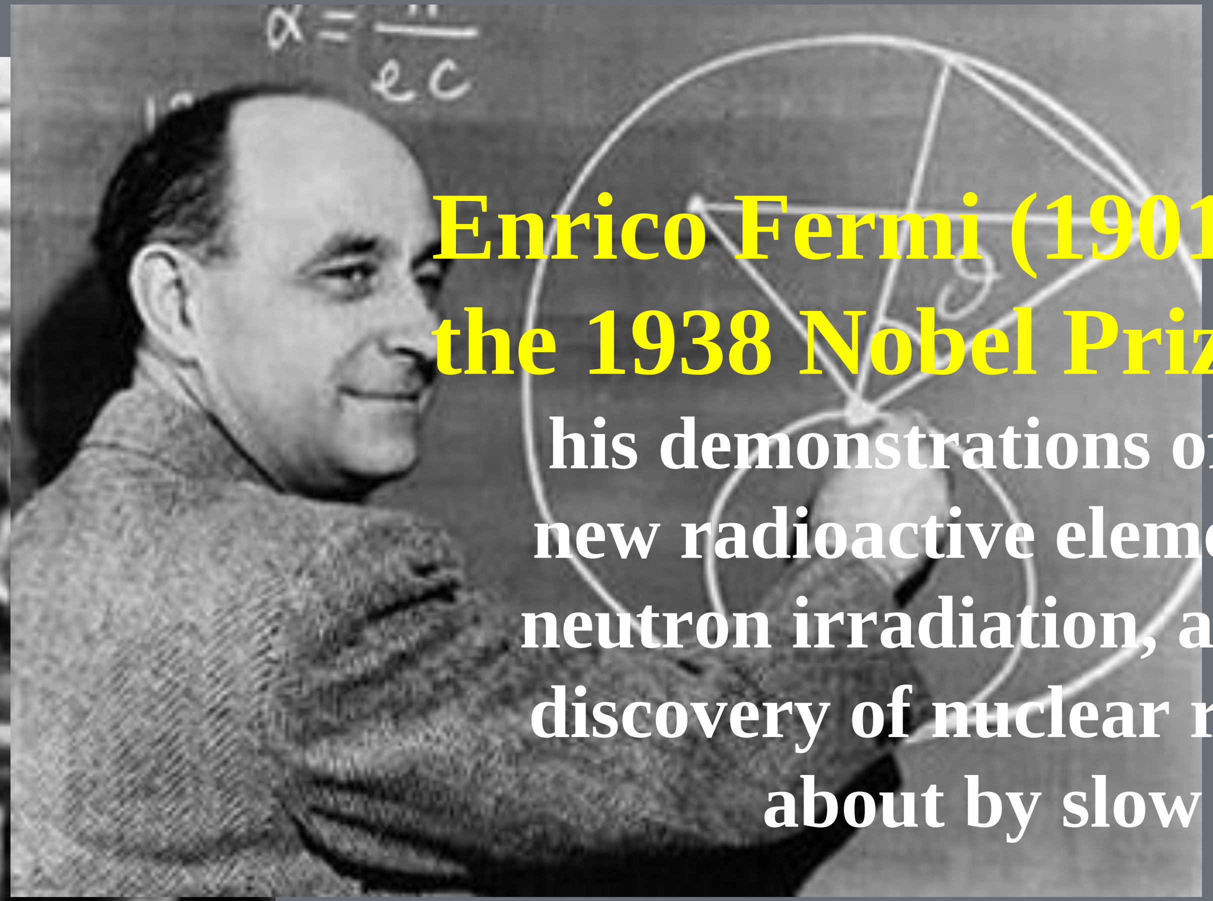
Nobel Prize in Chemistry, 1911 by the discovery of the elements radium and polonium

Nobel Prize in Chemistry, 1935: for the discovery of stable elements could artificially produce radioactive elements.

Nobel Prize in Chemistry, 1941, for the use of isotopes as tracers in the study of chemical processes

75th Chicago Pile-1 (CP-1) Commemoration

Manhattan Project
December 2, 1942
Chicago Pile - One (CP1)



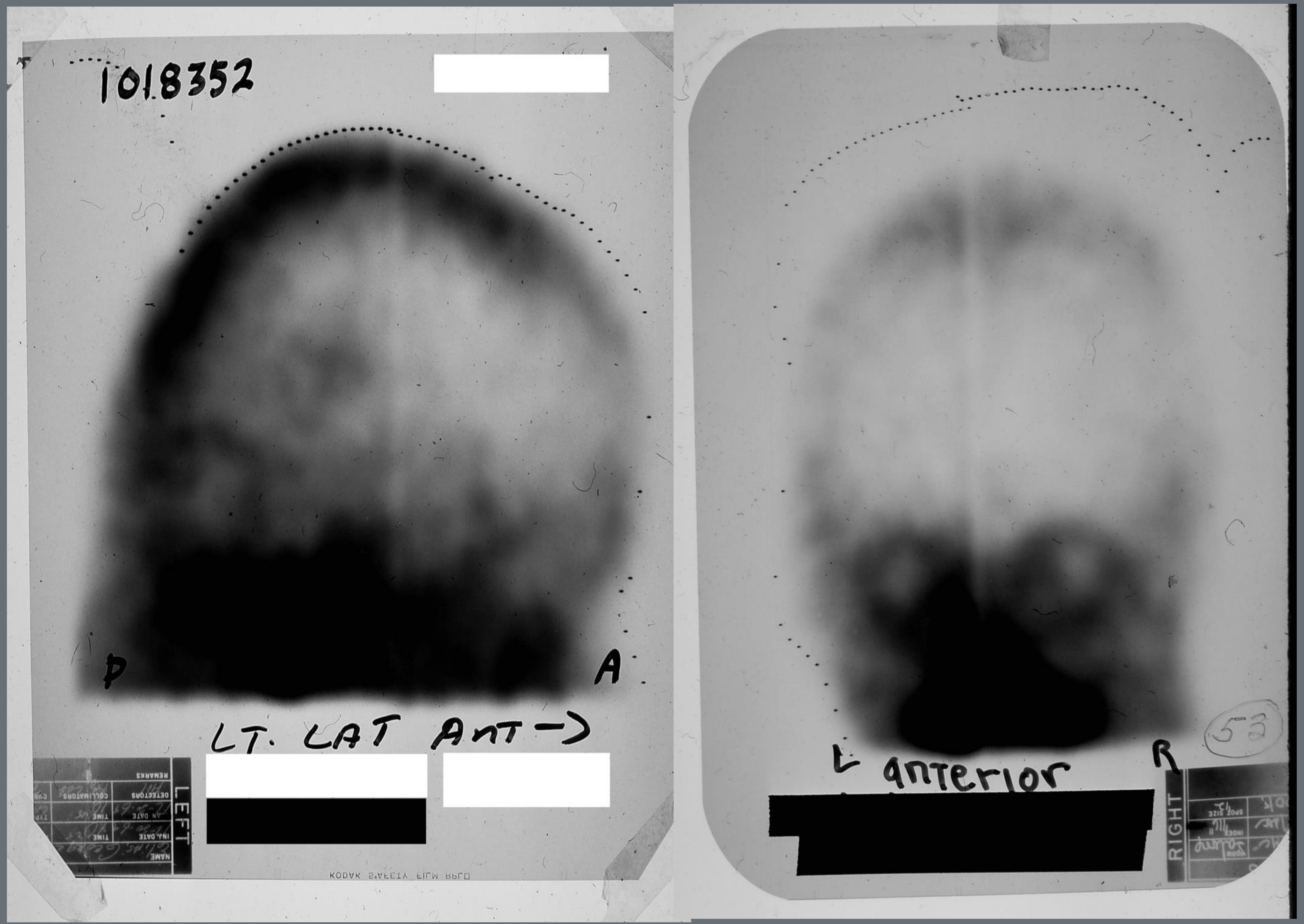
Enrico Fermi (1901-1954) received the 1938 Nobel Prize in Physics for **his demonstrations of the existence of new radioactive elements produced by neutron irradiation, and for his related discovery of nuclear reactions brought about by slow neutrons.**

On December 2, 1942
Man Achieved Here
The First Self-Sustaining
Chain Reaction
And Thereby
Initiated the
Controlled Release
of Nuclear Energy

Historic Evolution to Current Research

- *Post-WWII (1945)*
  "Atoms for Peace" Program
- *1953, Argonne Cancer Research Hospital (ACRH)*
  -- Peaceful Use of Atomic Energy in Medicine and Biology (both Diagnosis & Therapy)
- *1974, Franklin McLean Memorial Research Institute (FMI)*
  -- PET/SPECT
- *2005, Functional & Molecular Imaging Core (FMI)*
  -- Expanded into CT, Ultrasound, Optical Imaging, Emerging Technologies, Multi-Modality

Quantitative & Integrative Multi-Modality Functional & Molecular Imaging (QIM-FMI)



ACRH Brain Scanner

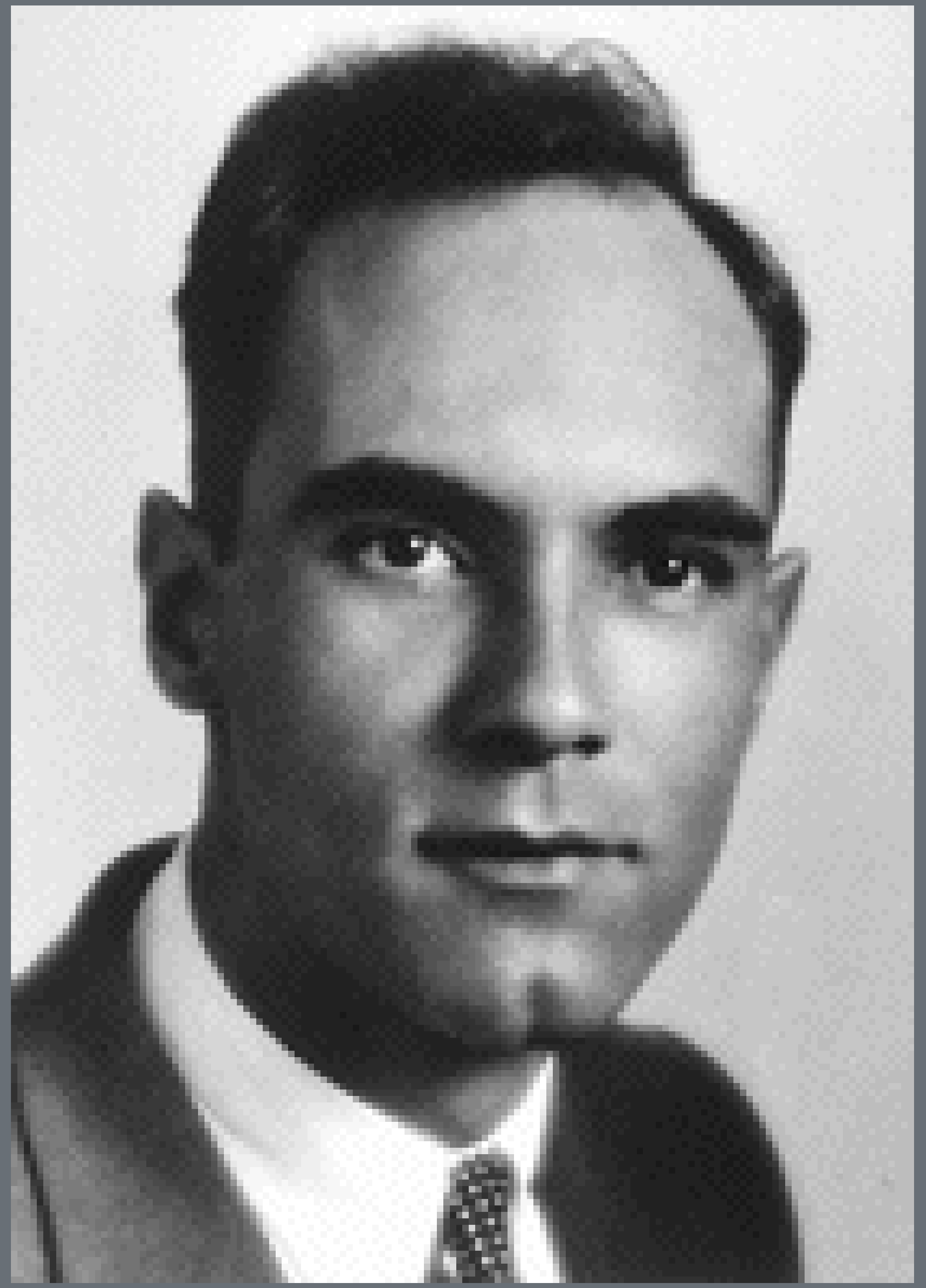
- *1962-63 The Birth of Modern Nuclear Medicine*
  First Tc-99m Brain Scan
  "First Molecular Image"

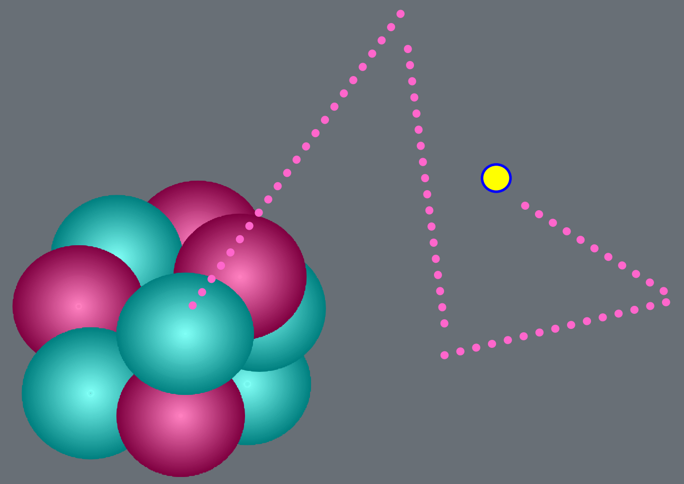
- *Multi-Disciplinary ACRH Molecular Imaging Team*
  Paul Harper (Surgeon)
  Robert Beck (Physicist)
  Katherine Lathrop (Chemist)
  Donald Charleston (Engineer)
  Alex Gottschalk(Radiologist)

World's First Tc-99m Brain Image, 1963

New Disciplines at Interfaces of
Biology, Medicine, Physics, Chemistry, Mathematics, Computer/Computing Science, Material Science/Engineering, Electrical Engineering + X

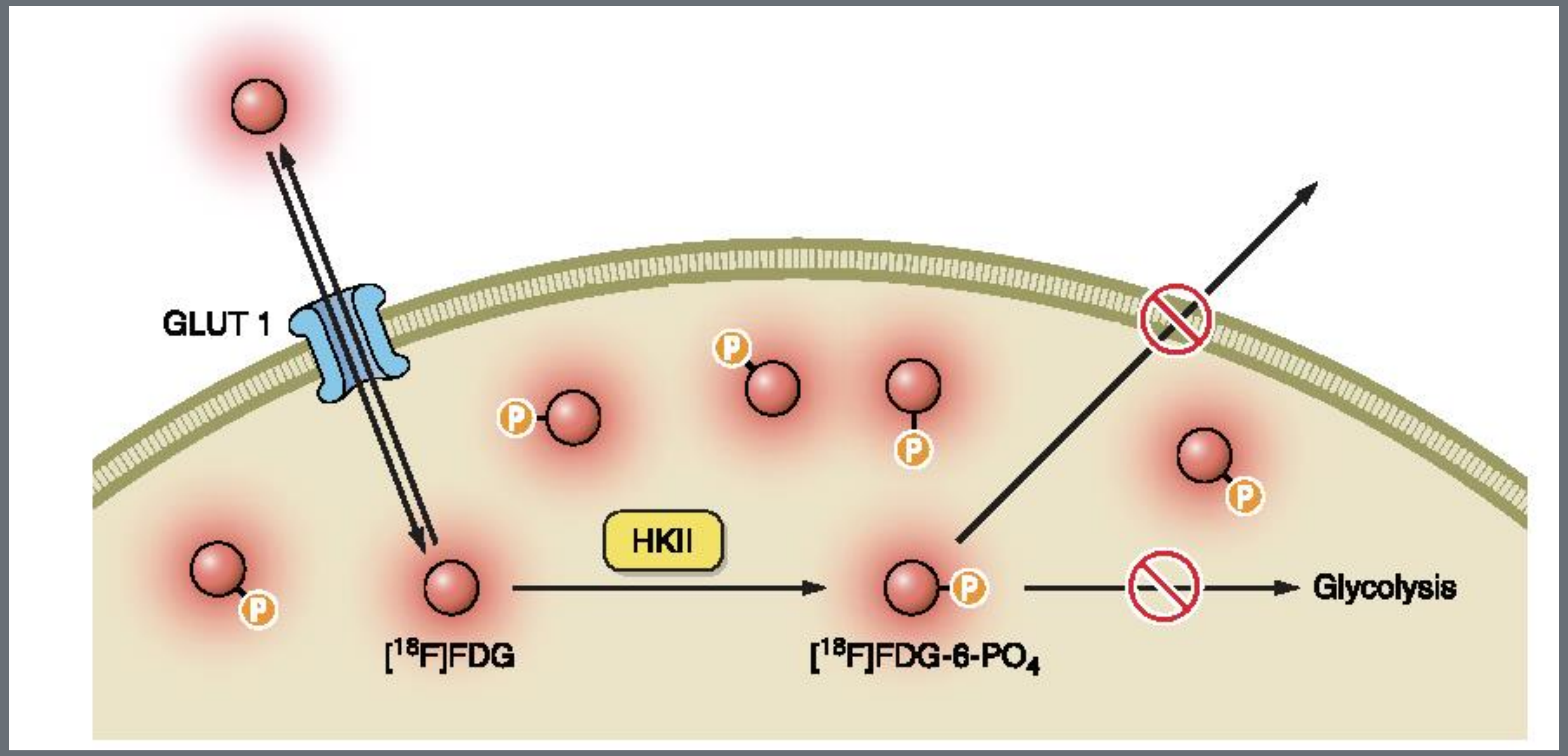
Positron Emission Tomography (PET): Principle

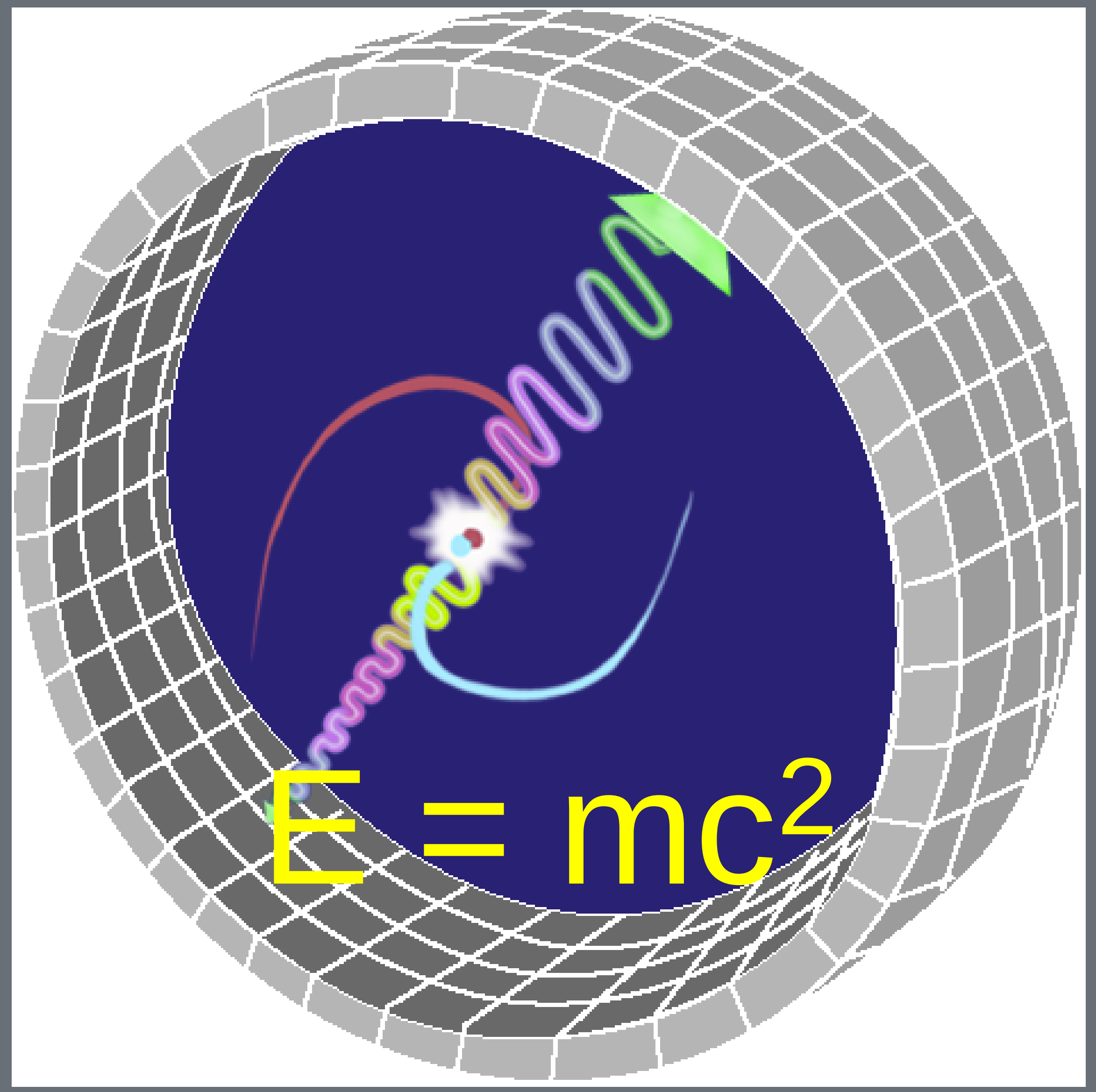




$$p \rightarrow n + e^{+} + \nu + \text{energy}$$

Carl David Anderson (1905-91) received the Nobel Prize in 1936 for the discovery of the positron.
At age 31, Anderson was then the youngest person to receive the Nobel Prize.



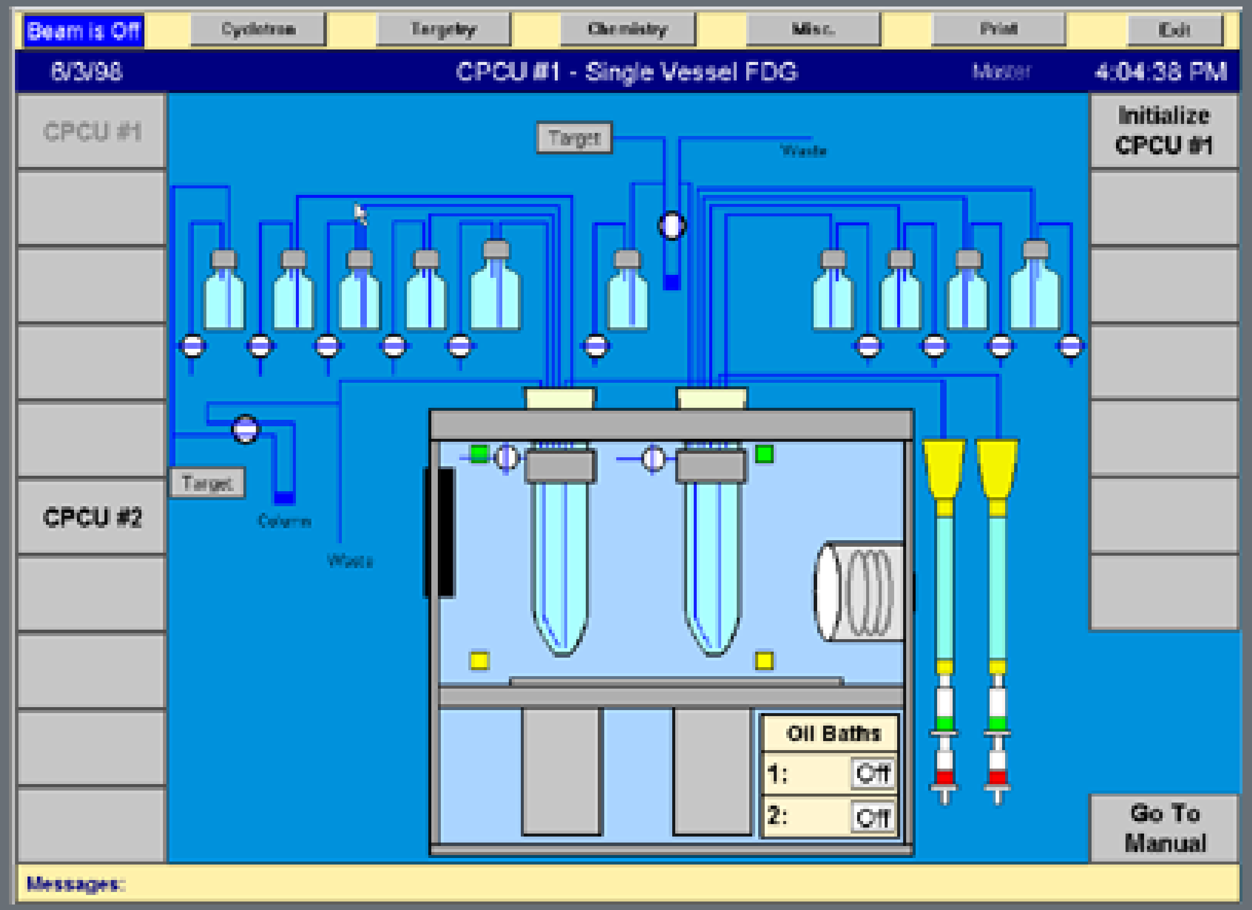


Positron-Emitting Nuclides

Isotope	Halflife	β^+ fraction	Max. Energy	range(mm)	production
C–11	20.4 mins	0.99	0.96 MeV	0.4 mm	cyclotron
N–13	9.96 mins	1.00	1.20 MeV	0.7 mm	cyclotron
O–15	123 secs	1.00	1.74 MeV	1.1 mm	cyclotron
F–18	110 mins	0.97	0.63 MeV	0.3 mm	cyclotron
Cu–62	9.74 mins	0.98	2.93 MeV	2.7 mm	generator
Cu-64	12.7 hours	0.19	0.65 MeV	0.3 mm	cyclotron
Ga–68	68.3 mins	0.88	1.83 MeV	1.2 mm	generator
Br-76	16.1 hours	1.00	1.90 MeV	1.2 mm	cyclotron
Rb–82	78 secs	0.96	3.15 MeV	2.8 mm	generator
I–124	4.18 days	0.22	1.50 MeV	0.9 mm	cyclotron

Production of Isotopes (Cyclotron)

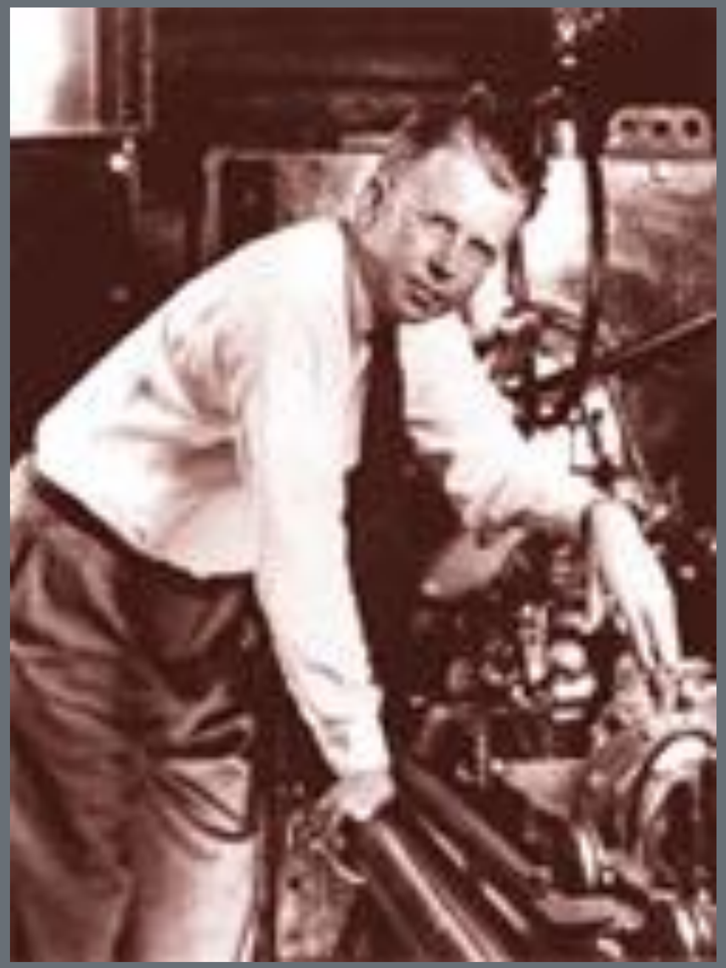
Modern Medical Cyclotron



RadioChem Synthesis Module

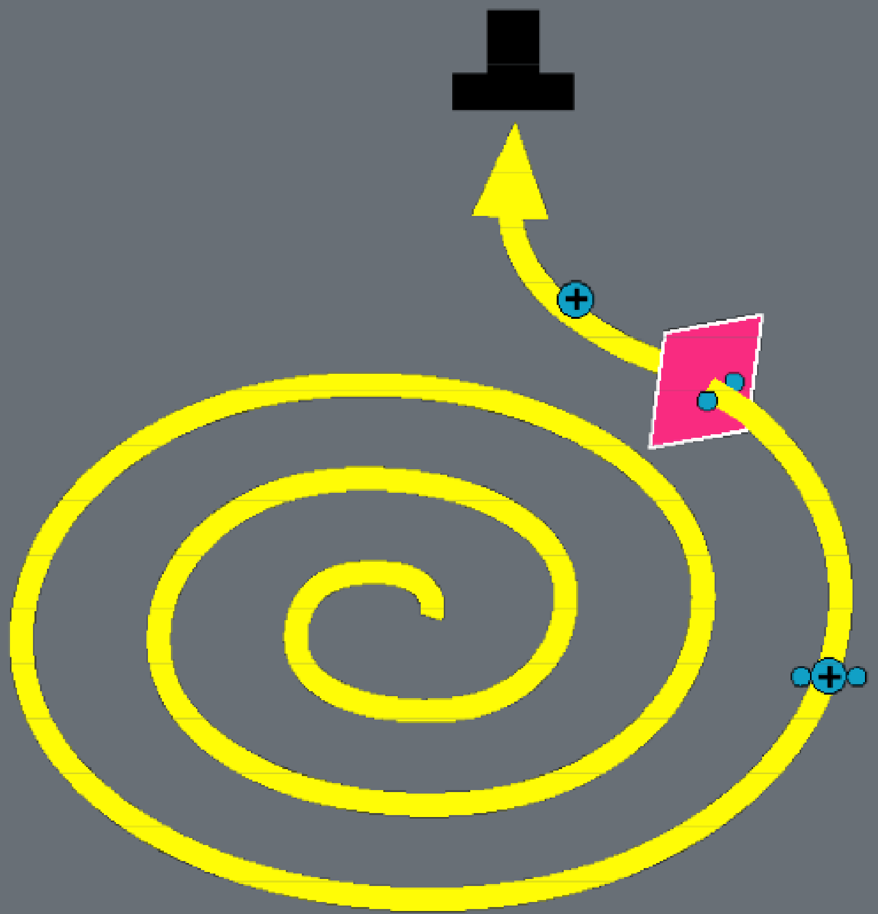
UChicago new cyclotron and radiochemistry facilities (2017)

Production of Isotopes (Cyclotron)

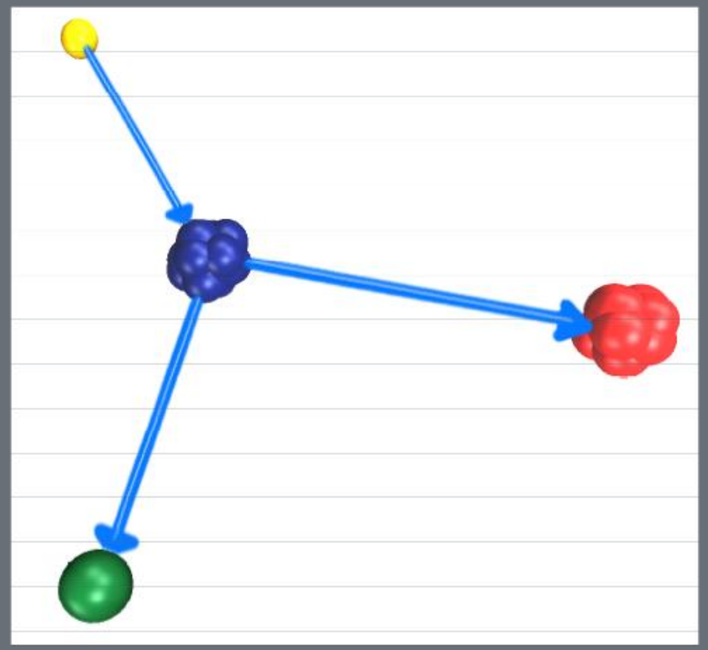


At the ion source of the 184-inch cyclotron in 1948.

The first cyclotron is built in late 1930



$^{18}O\ (p,n)\ ^{18}F$



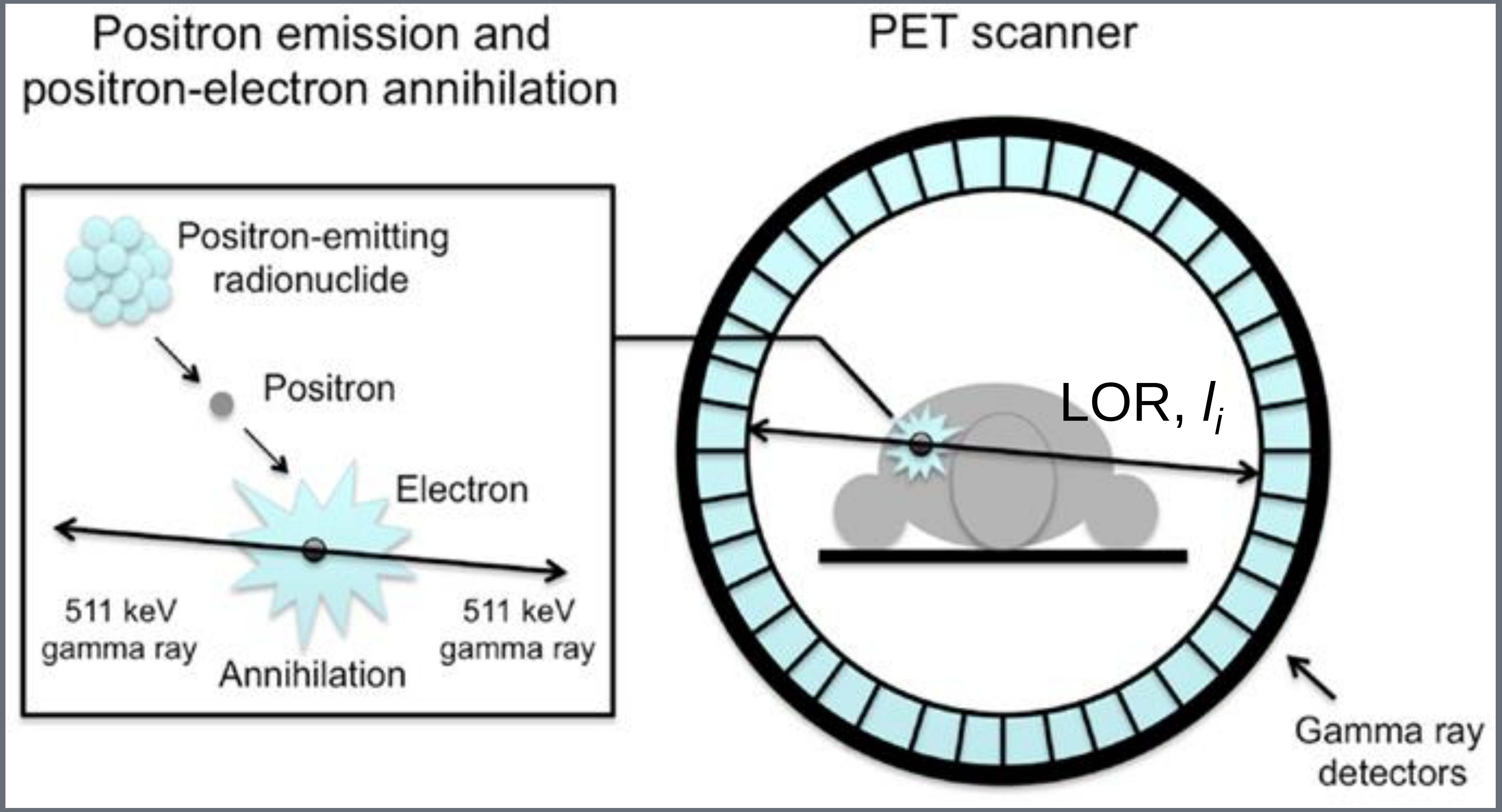
Lawrence at the Controls of his cyclotron in Berkeley.

Ernest Orlando Lawrence (1901-1958) received the 1939 Nobel Prize in physics for the invention and development of the cyclotron

CS-15 Installed at UChicago-ACRH/FMI in 1968

Positron Emission Tomography (PET): Principle

Coincidence Detection

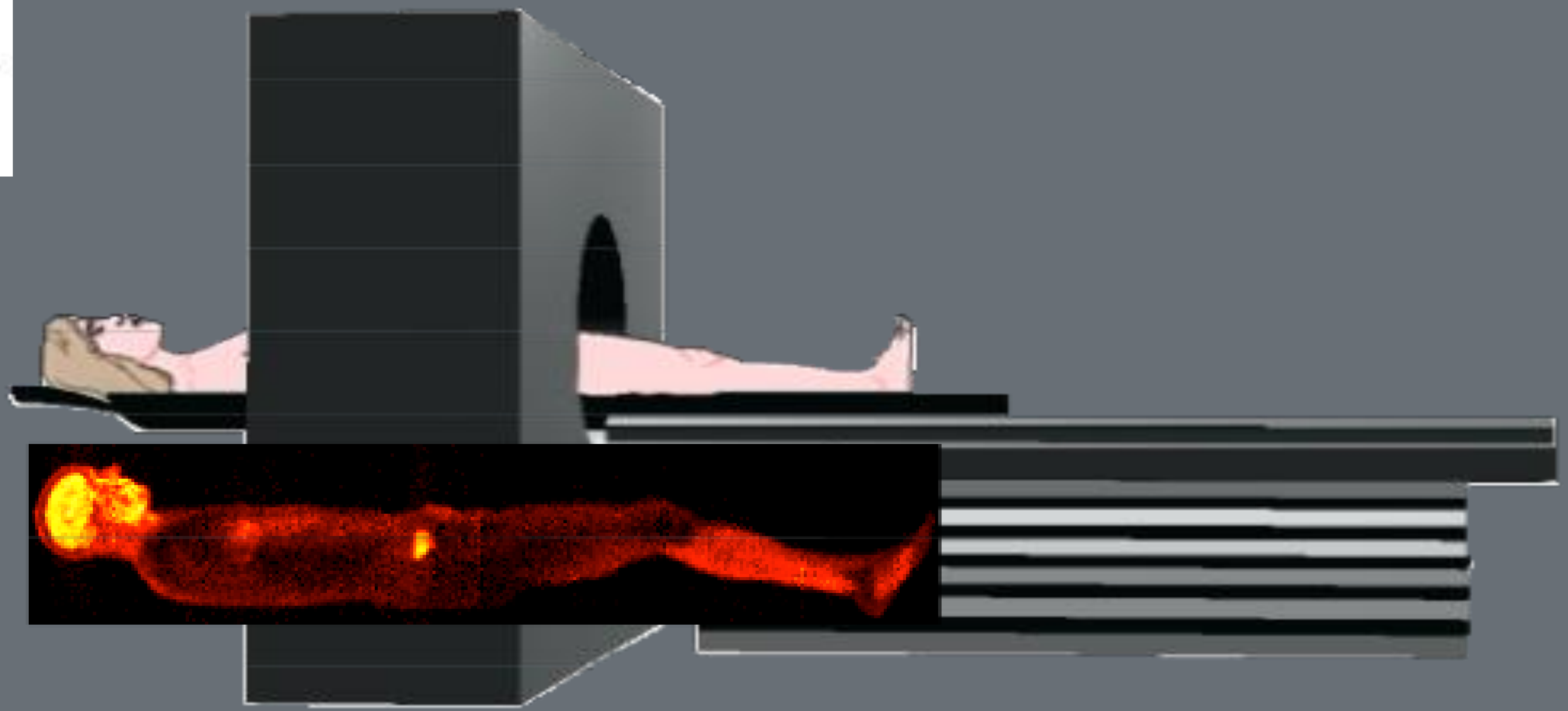


$$t_i = \epsilon_i a_i \times \boxed{\int_{l_i} f(\vec{r}\,)dl}$$

line integral
/ray sum

LOR sensitivity
(calibration)

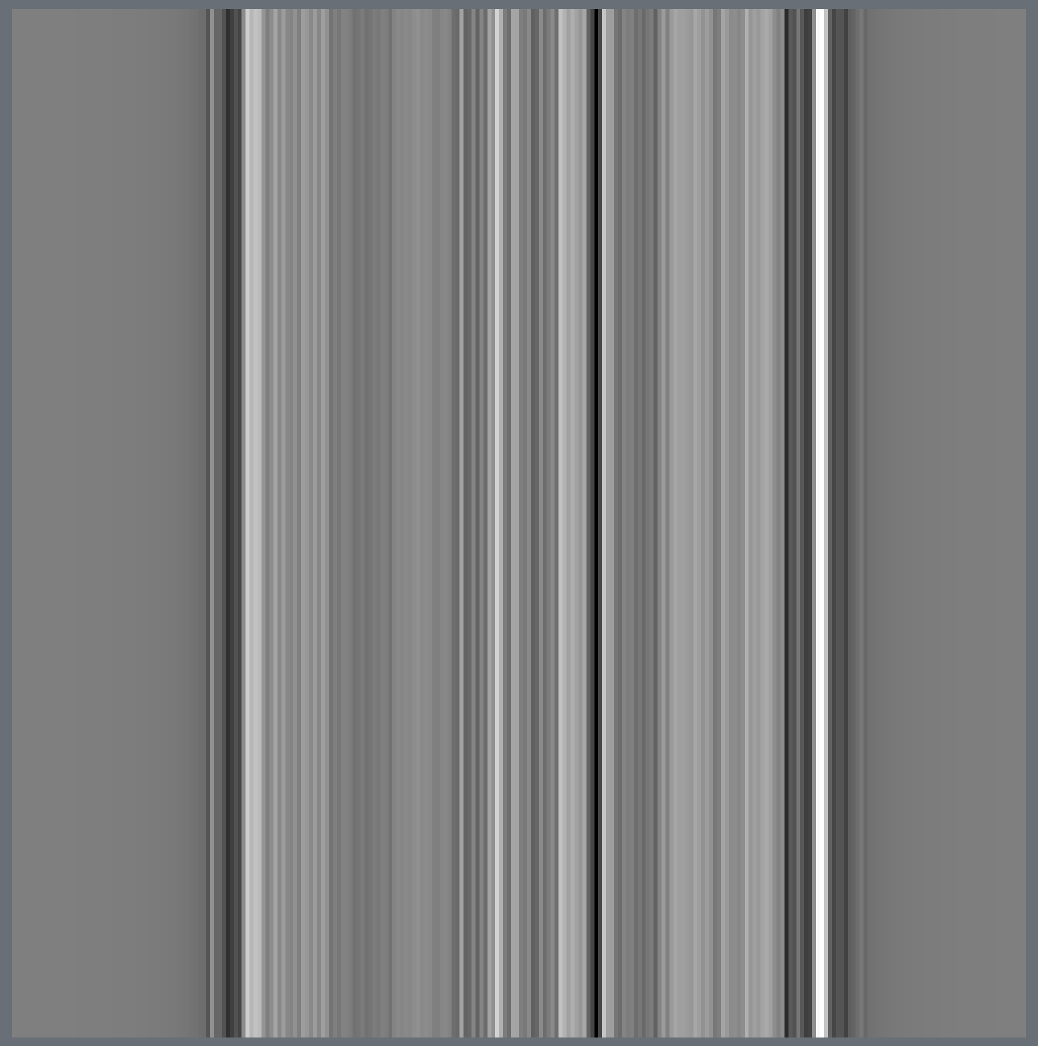
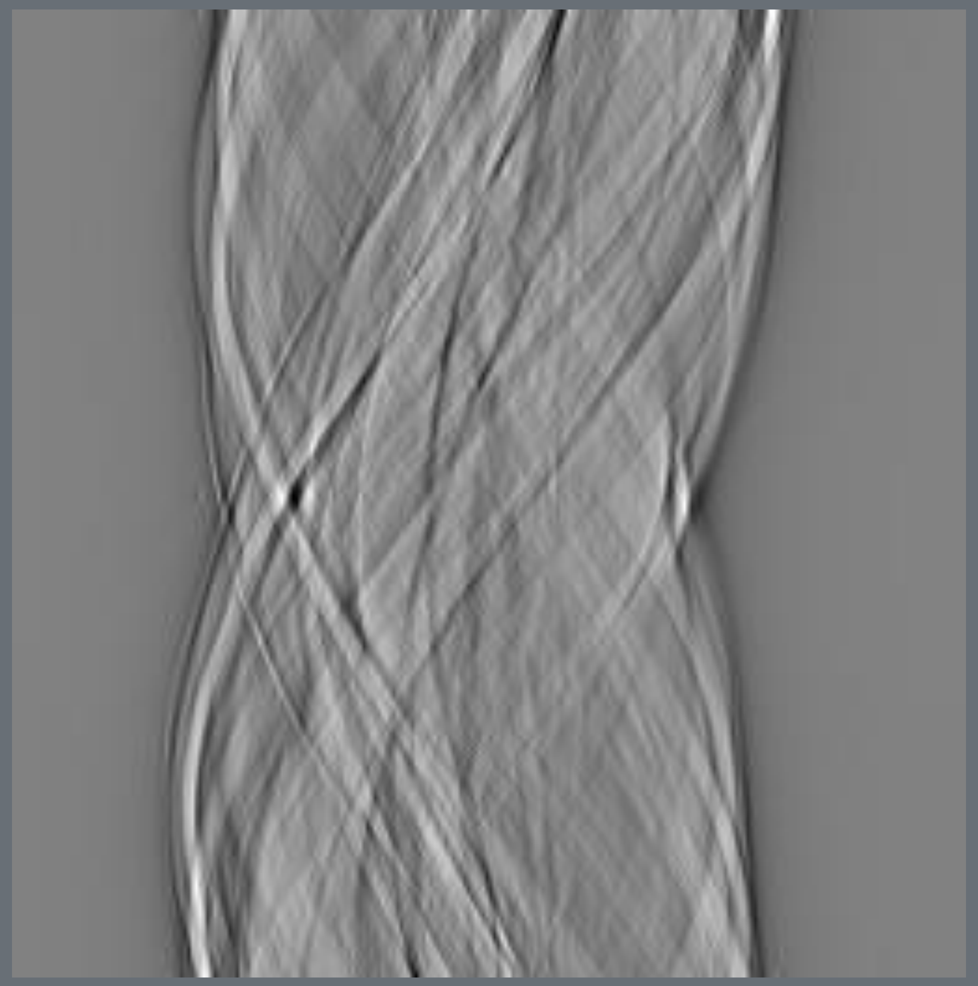
subject attenuation
(measured using a tx source, or calculated from CT, MR images)



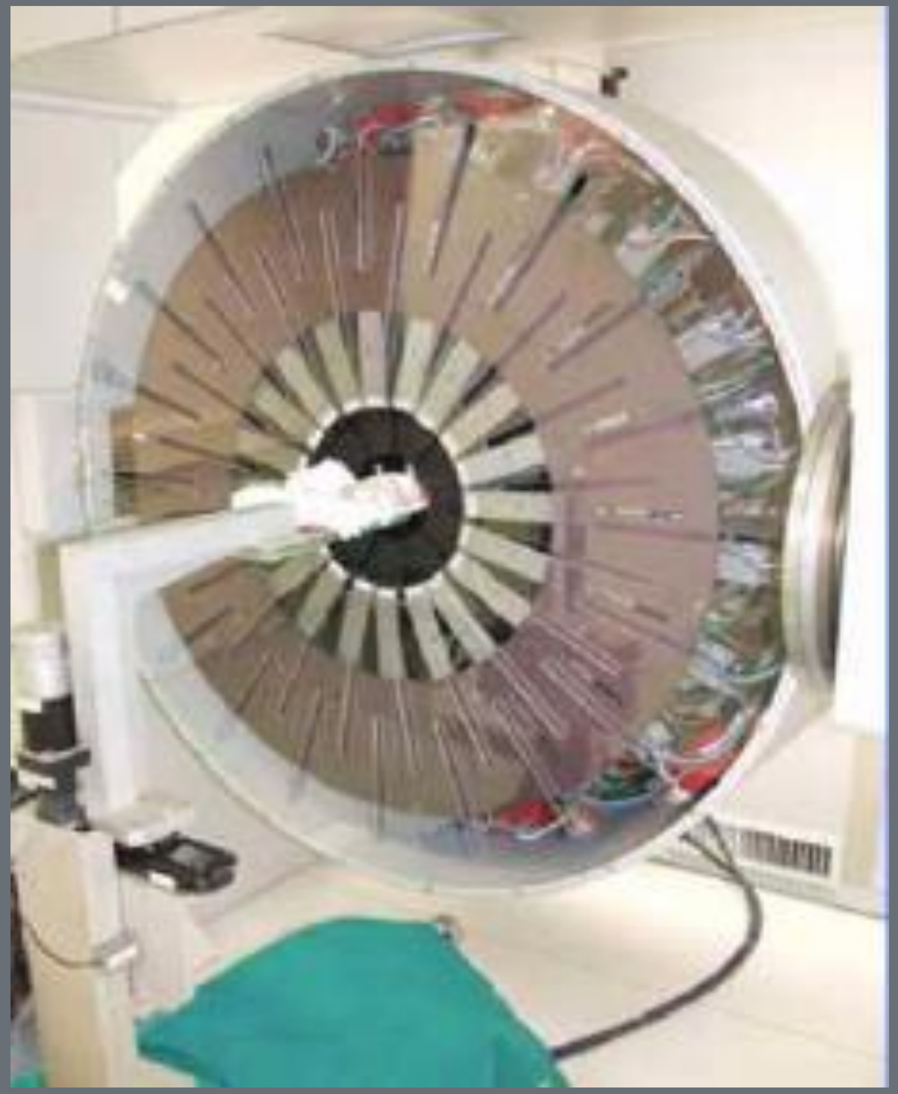
Positron Emission Tomography (PET): Principle

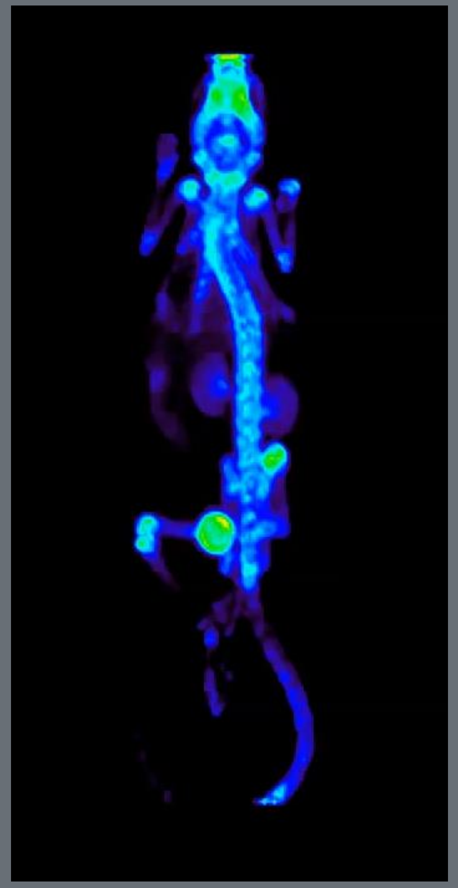
Image Reconstruction from projections:
2D FBP Demonstration



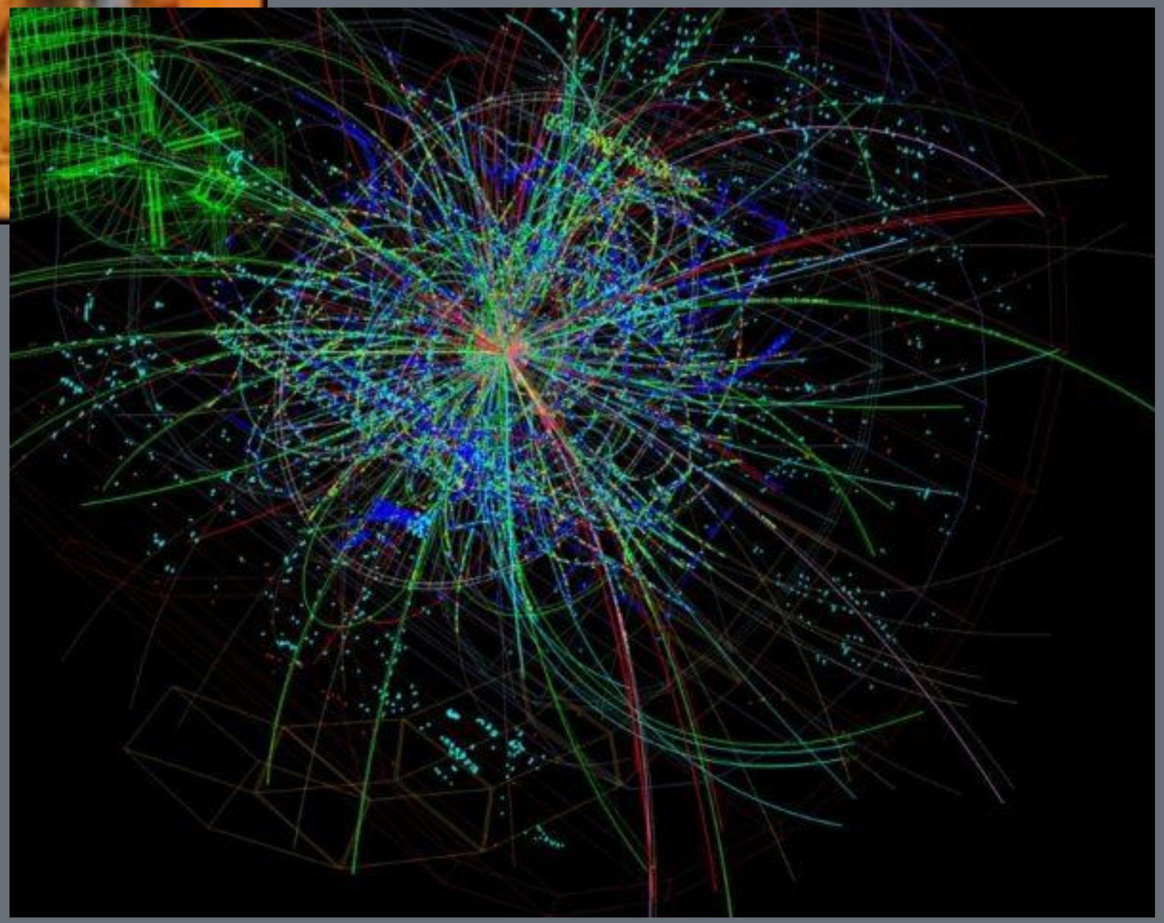



PET system

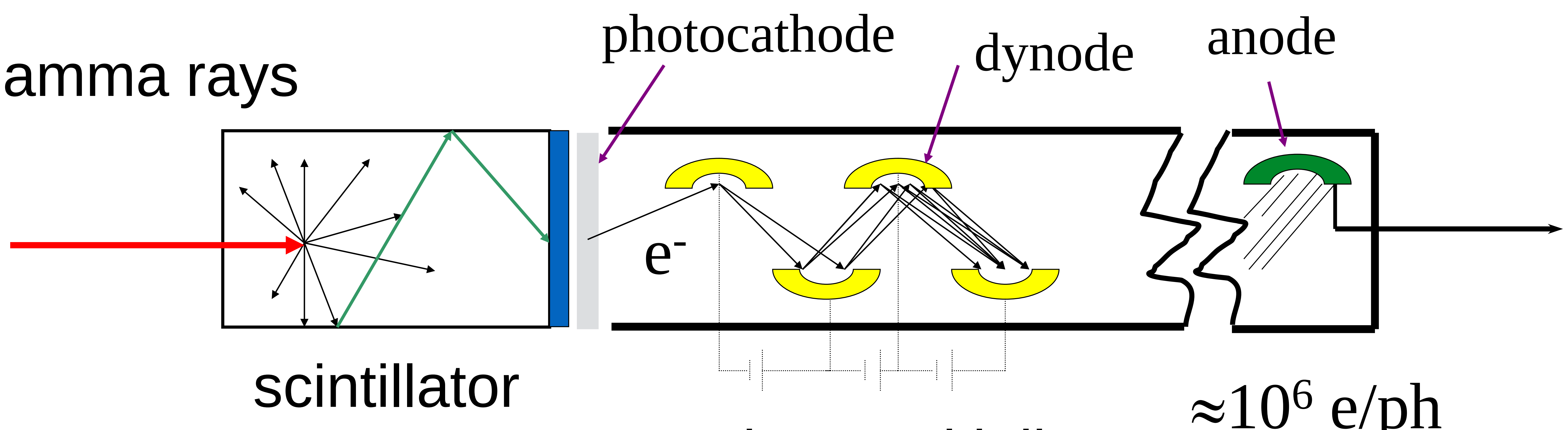


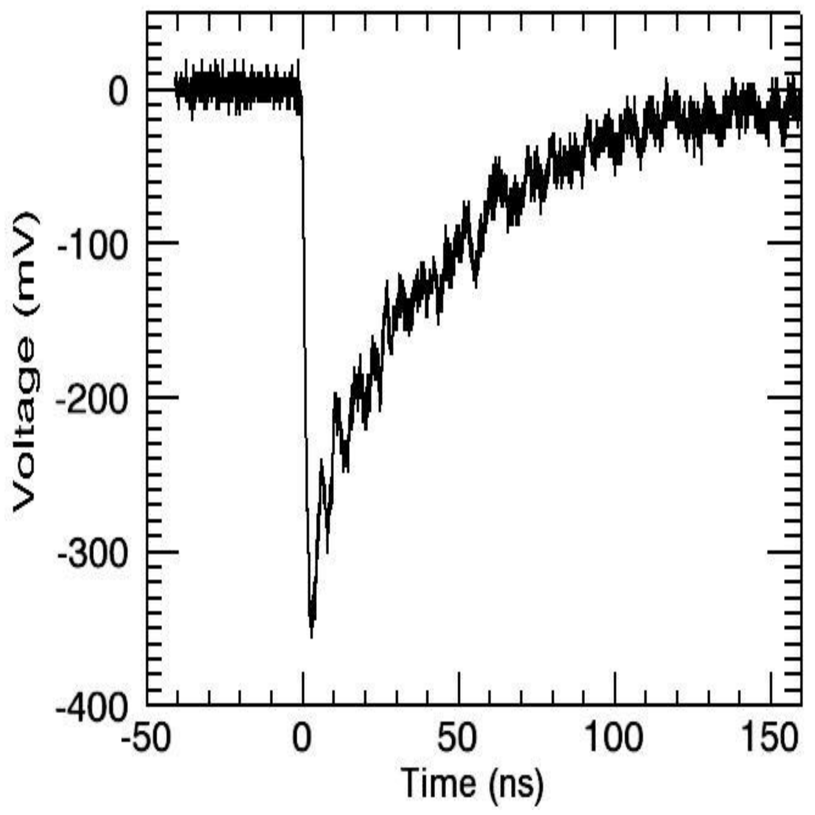


Share similar designs with HEP detectors but subject to different size and cost constraints and performance requirements

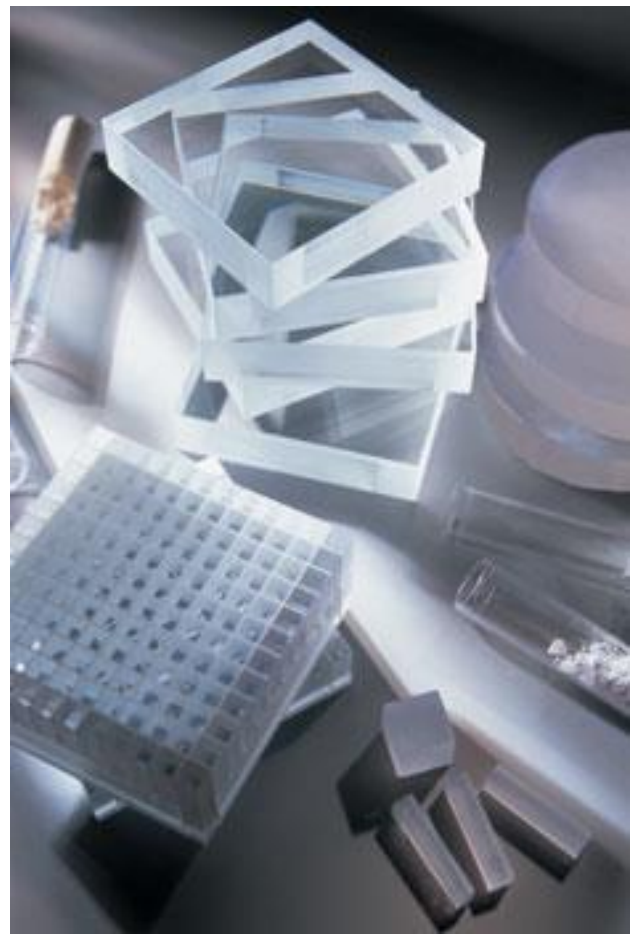


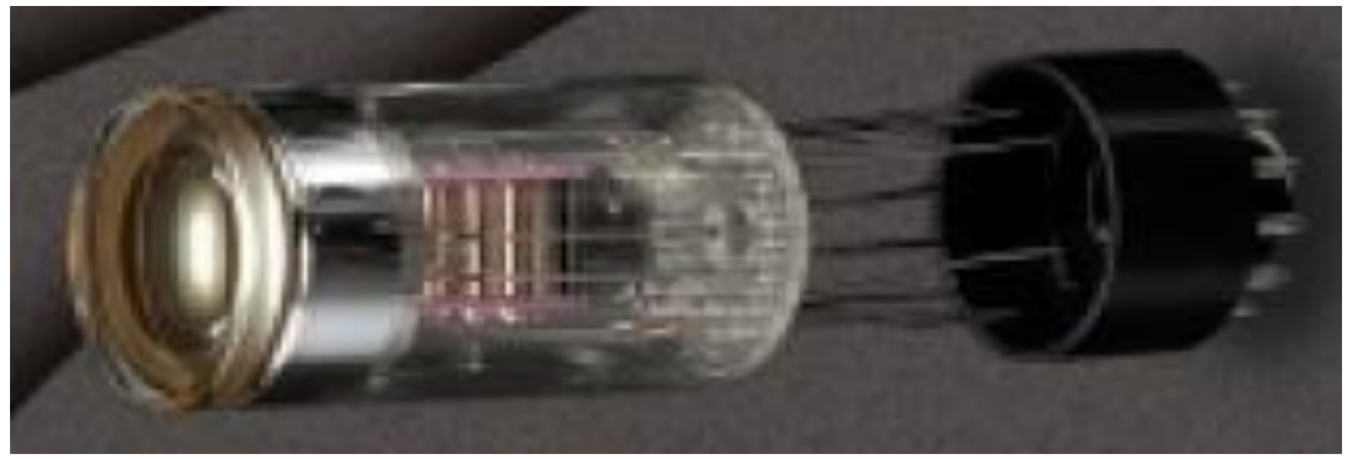
Scintillation Detector



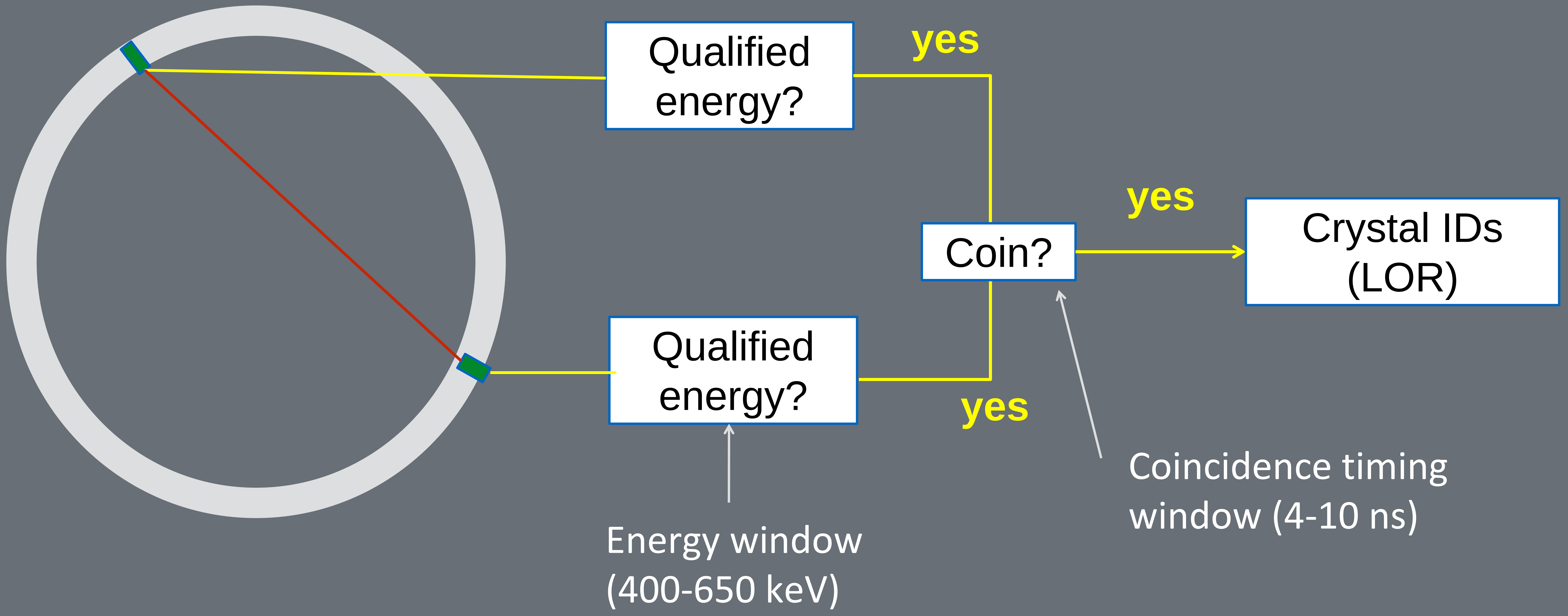


electrical signal
- time
- energy

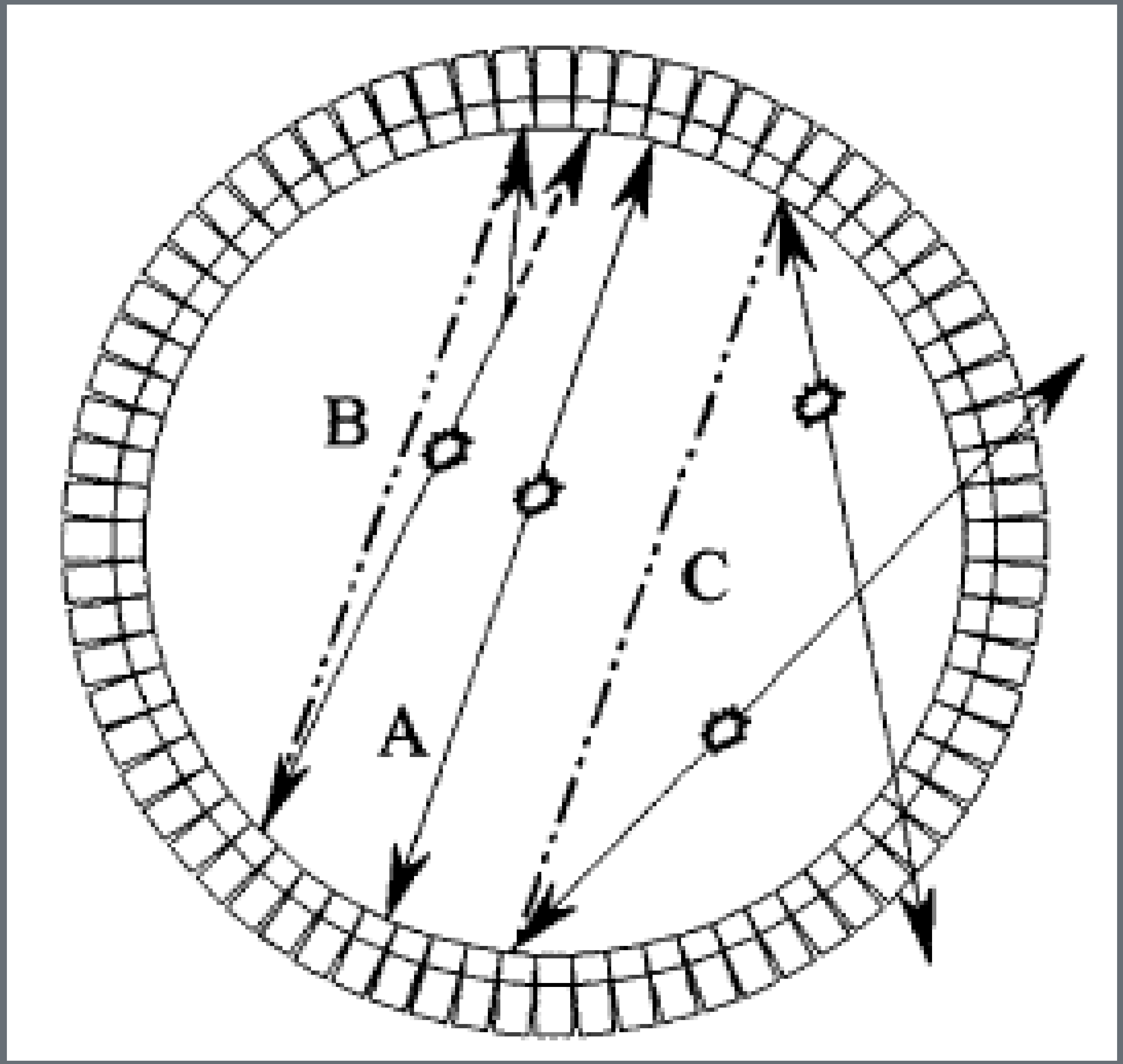




PET Event Detection



PET Event Types



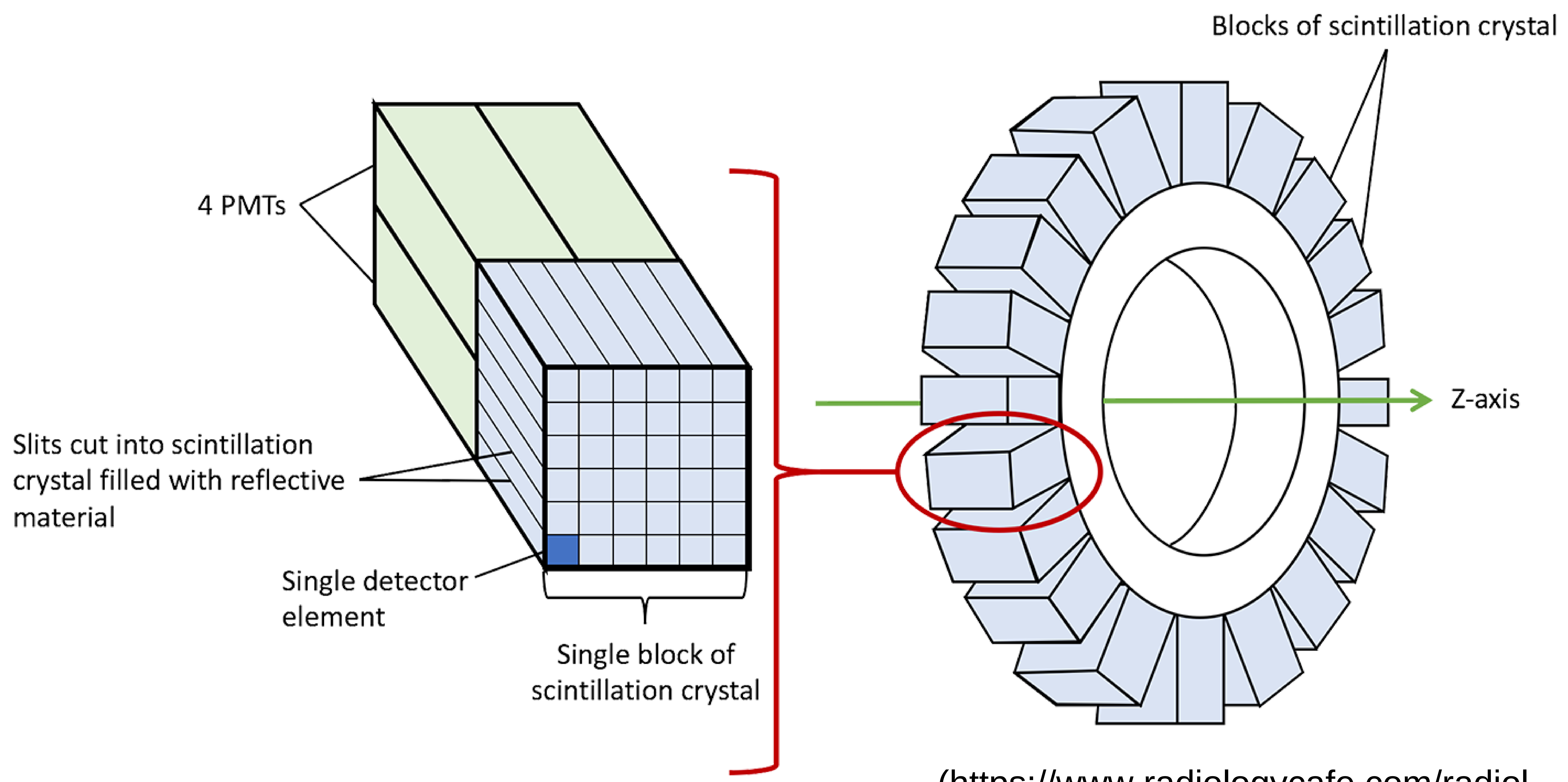
Scatter (B)

- Compton scattering in subject
- energy <511 keV
- depend on object size and scanner geometry
- distribution affected by subject shape
- cannot be easily measured

Randoms (C)

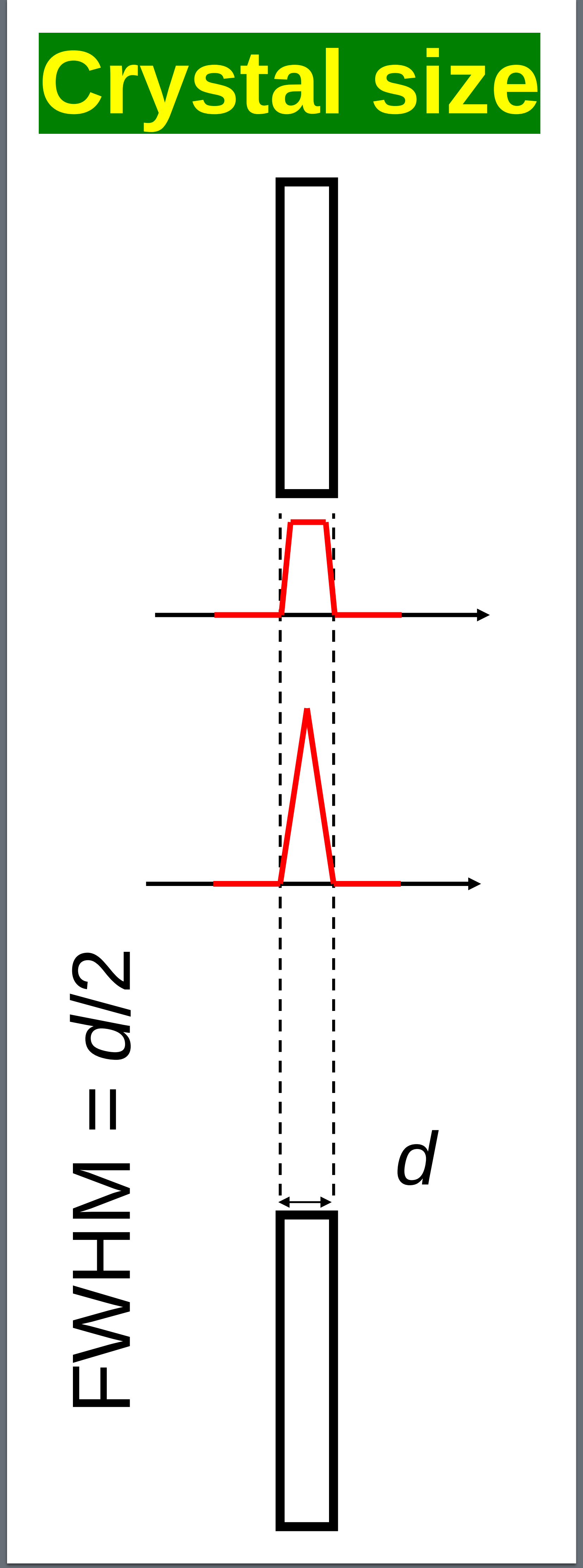
- accidental coincidences
- smaller coincidence windows → fewer randoms depend on activity levels
- relatively uniform distribution
- can be measured using delayed coincidences

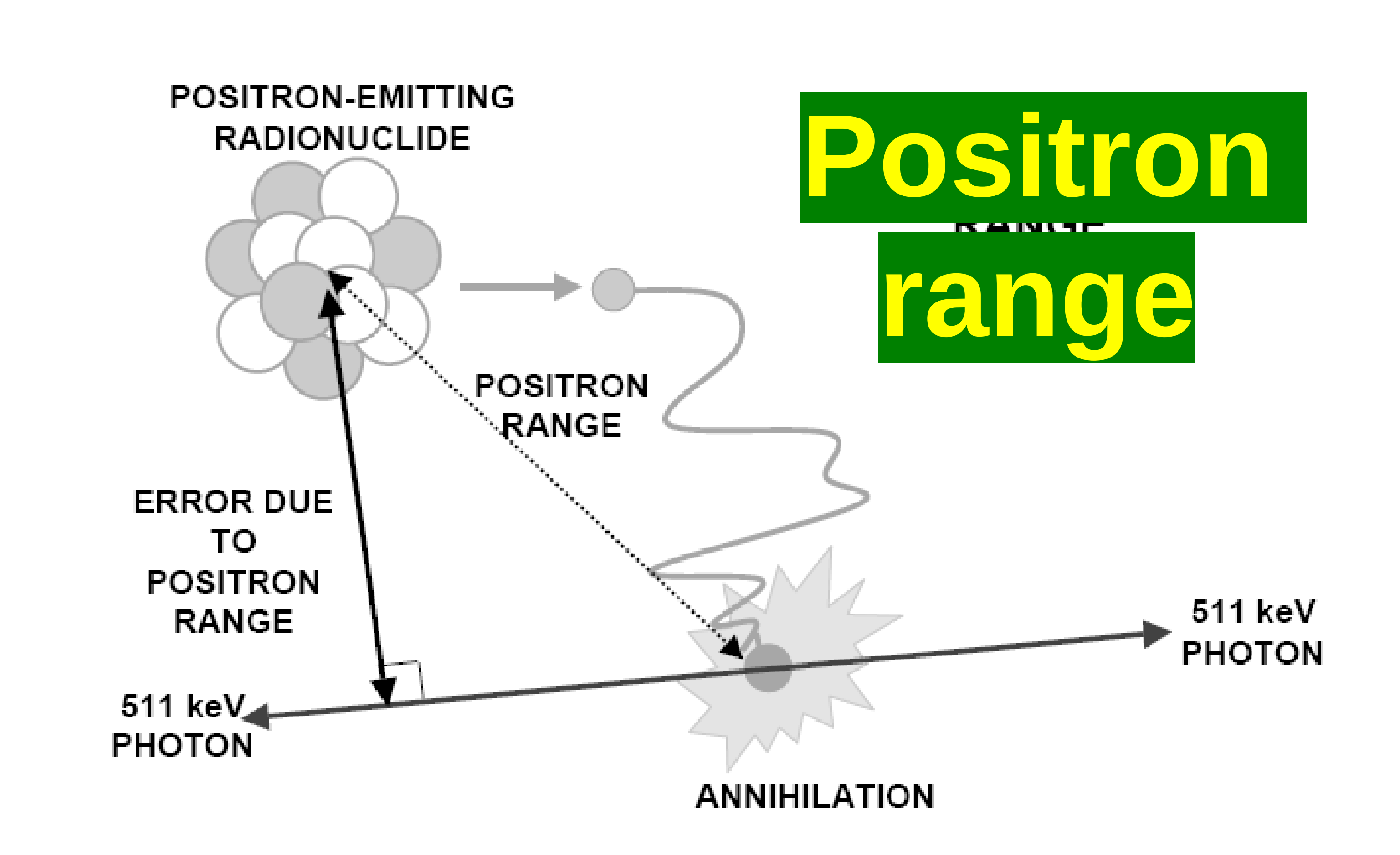
PET Block Detector



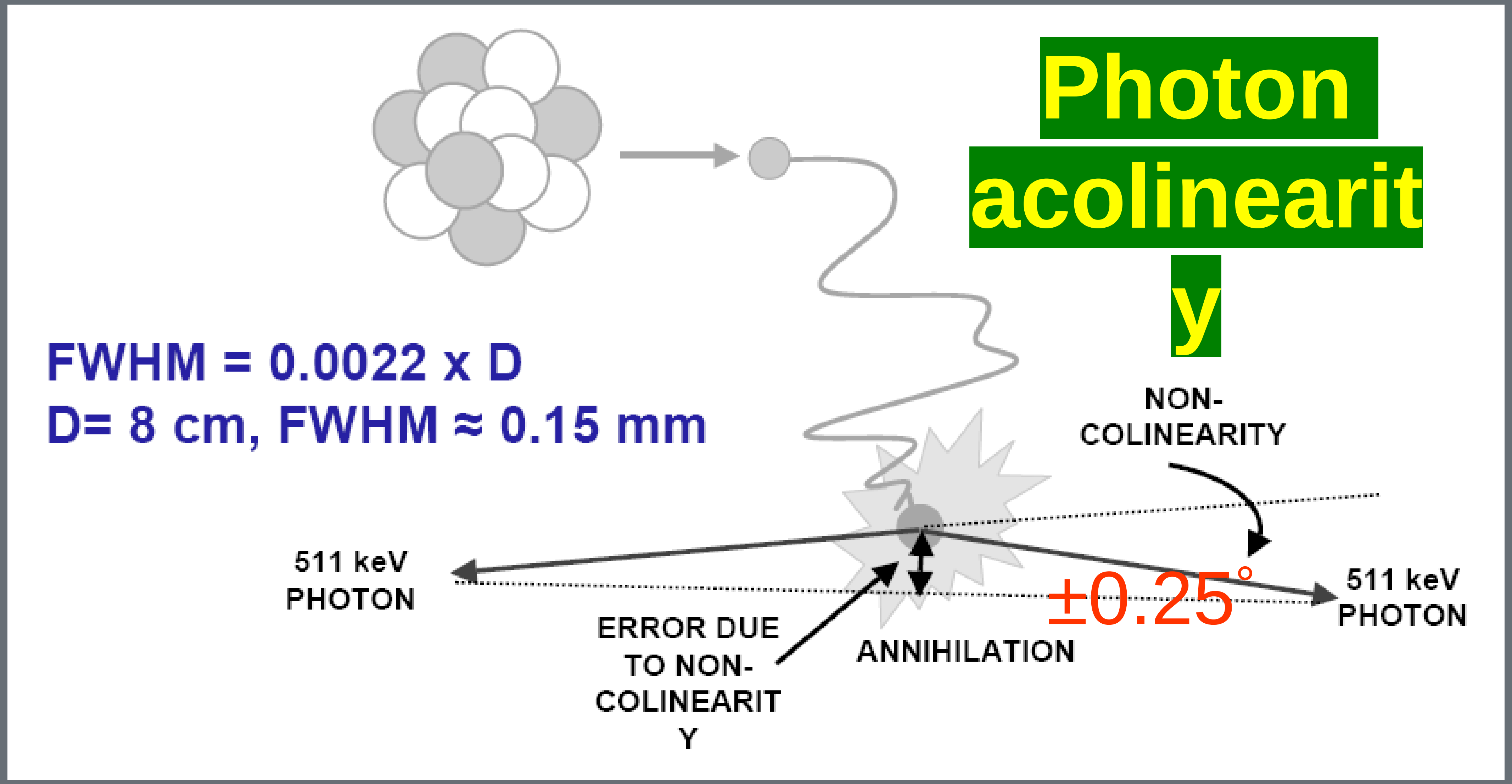
(https://www.radiologycafe.com/radiology-trainees/frcr-physics-notes/pet-imaging)

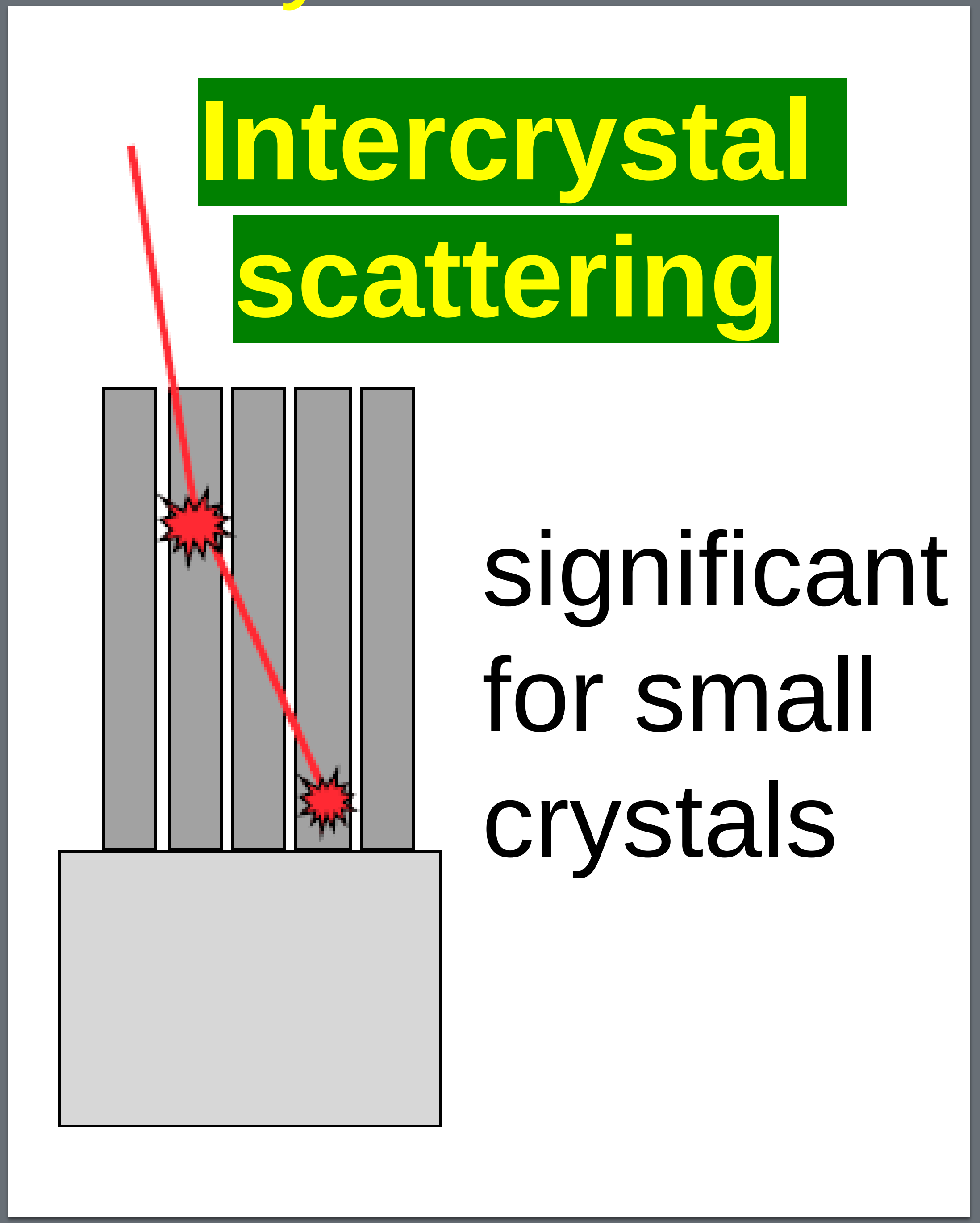
Factors affecting resolution





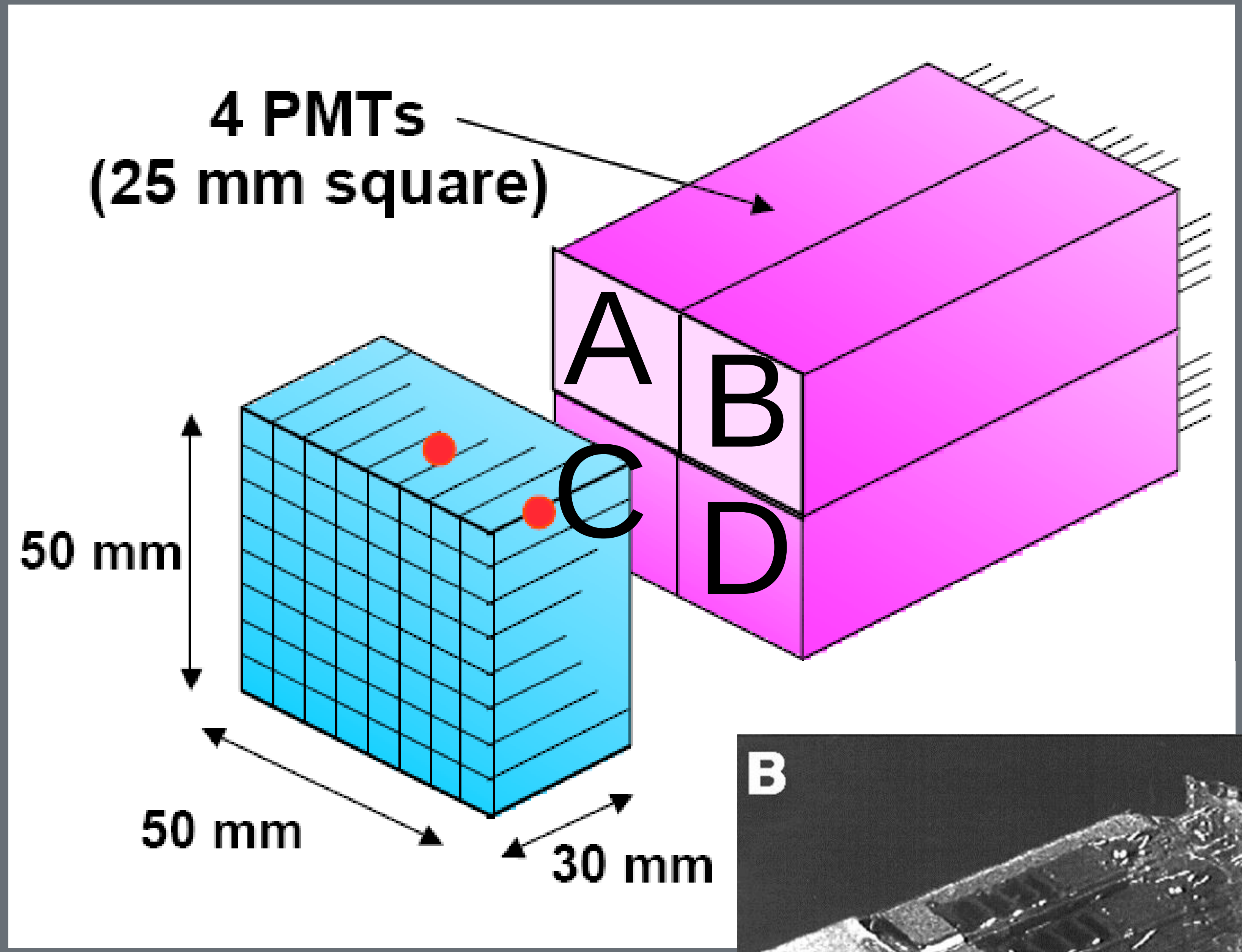
- depends on E_{max} of emitted positrons
  - ^{18}F rms = 0.23 mm
  - ^{11}C rms = 0.39 mm
- range is inversely proportional to the absorber density

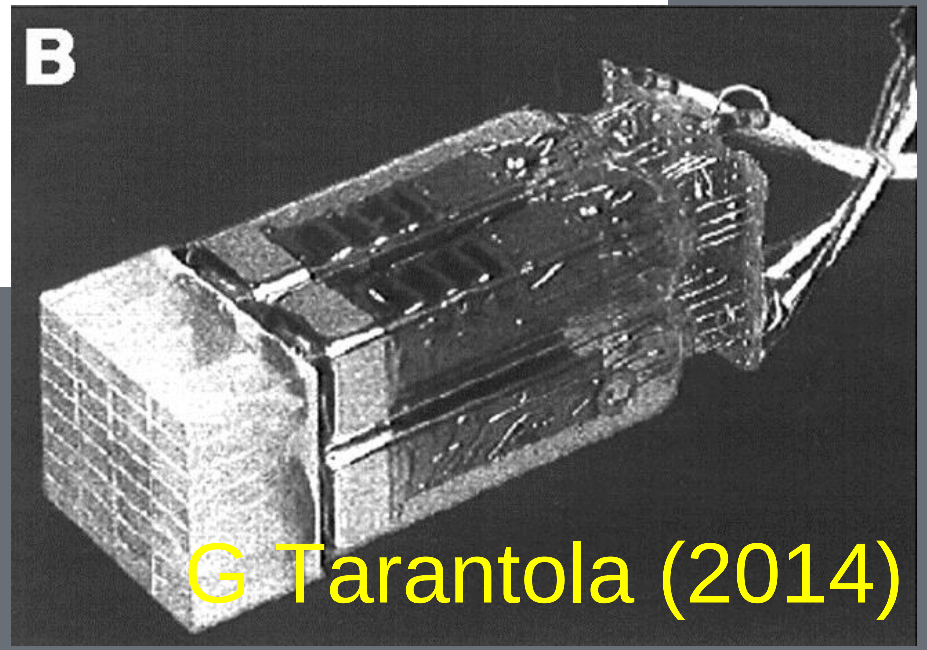


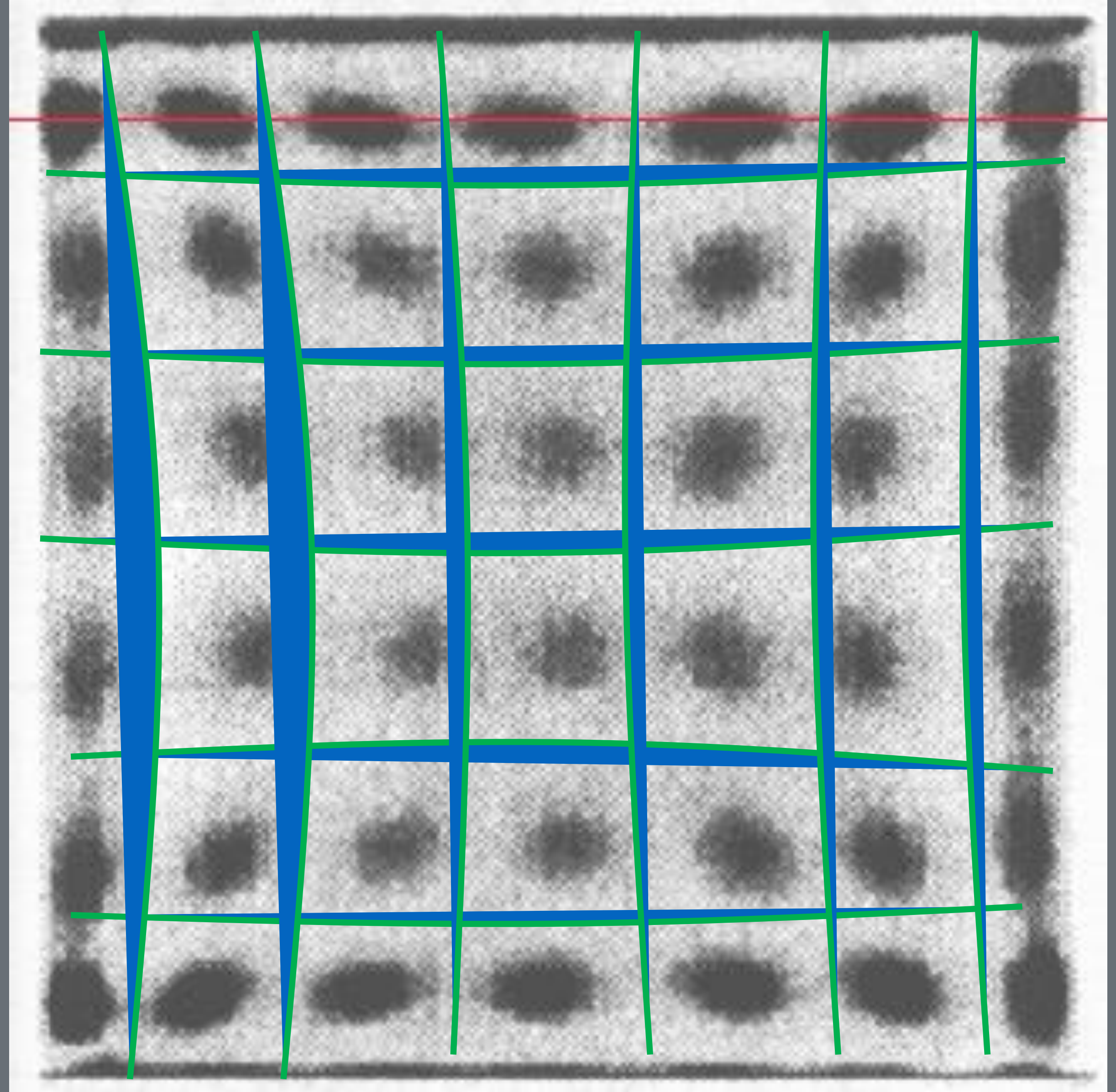


Block Detectors

Clinical PET: 4 mm detector pixels, ~80 cm diameter, 20 cm length ➔ 31,400 pixels







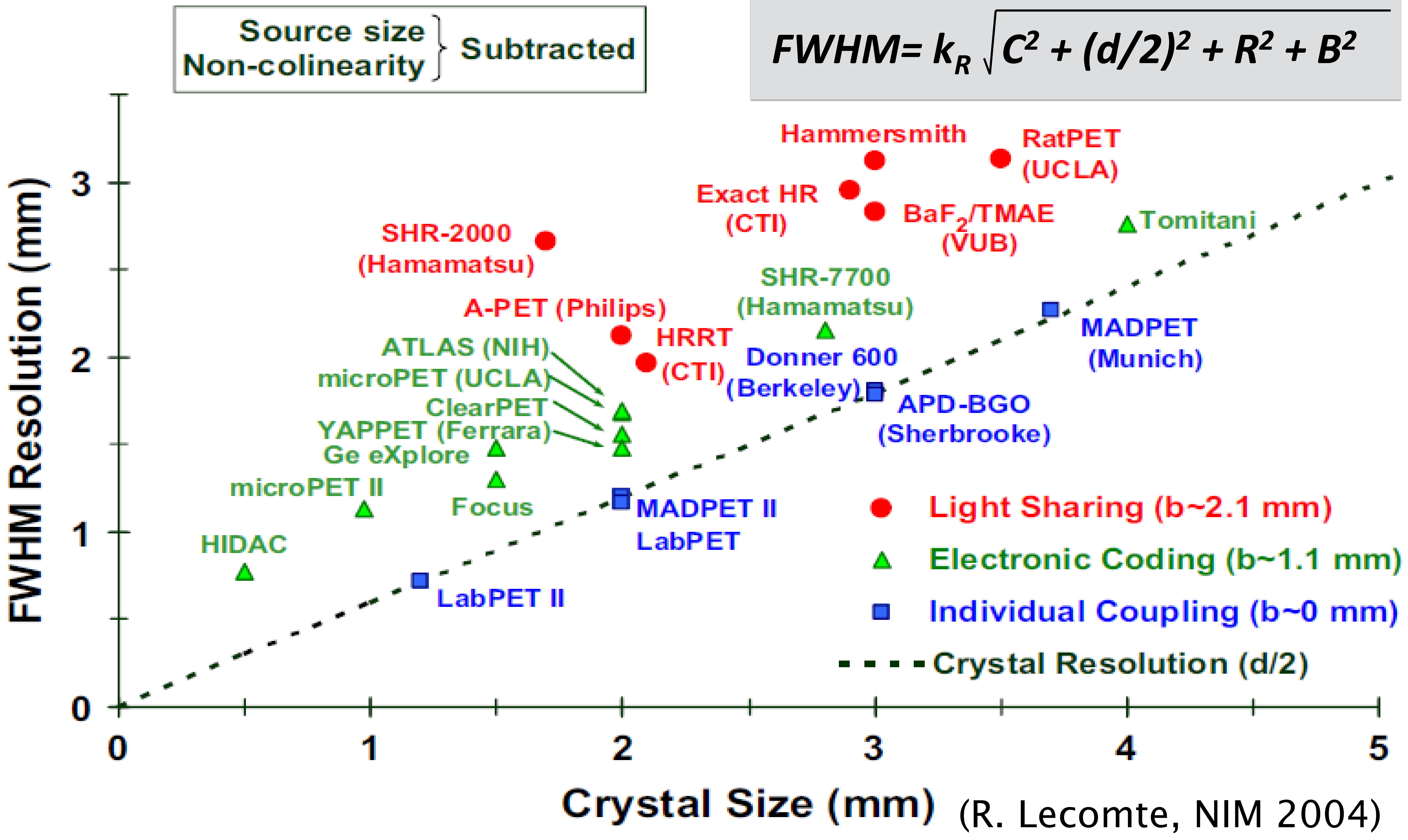
$$x = \frac{B+D}{A+B+C+D}$$

$$y = \frac{A+B}{A+B+C+D}$$

- Event energy (pulse height) and time are derived from the summed pulse, assuming only one event within the processing time
- Compromised count-rate capability
- More lights (brighter scintillators and better light collection) → better statistics → better energy resolution, better spatial resolution, better timing
- Faster scintillator and PMTs → faster timing

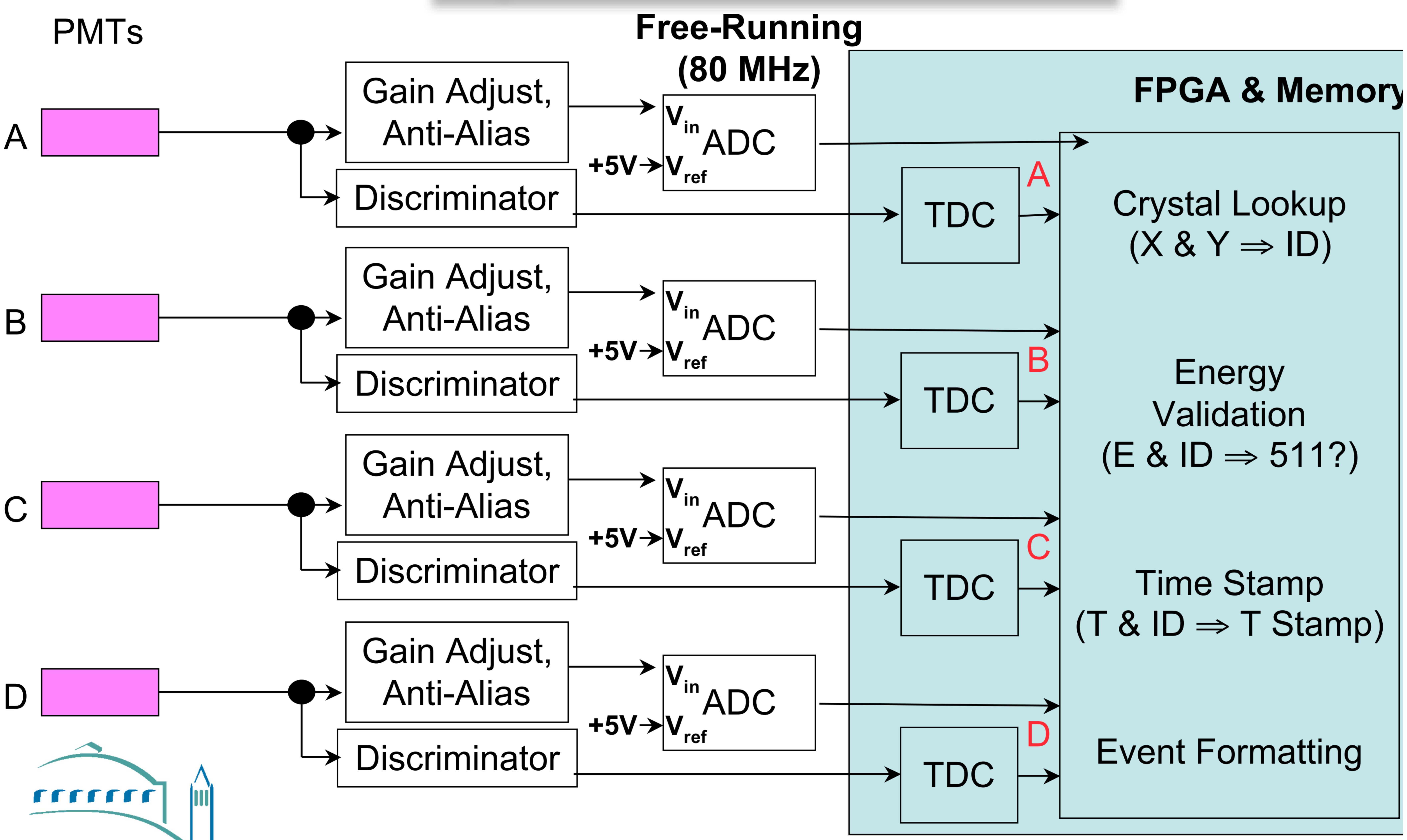
8x8 block detectors ➔ reduce electronic channels by x16

$$FWHM = k_R \sqrt{C^2 + (d/2)^2 + R^2 + B^2}$$



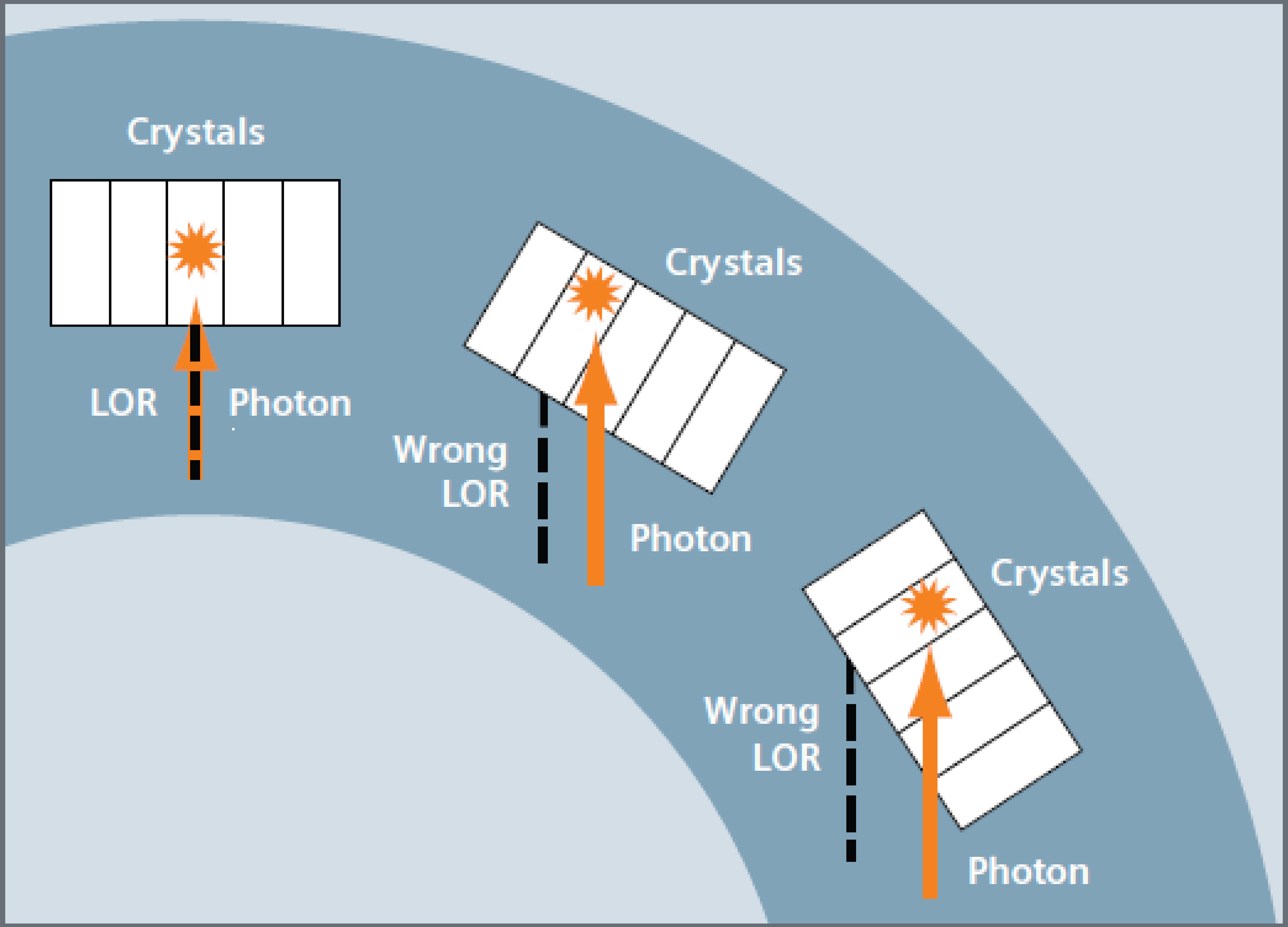
(R. Lecomte, NIM 2004)

OpenPET Front End



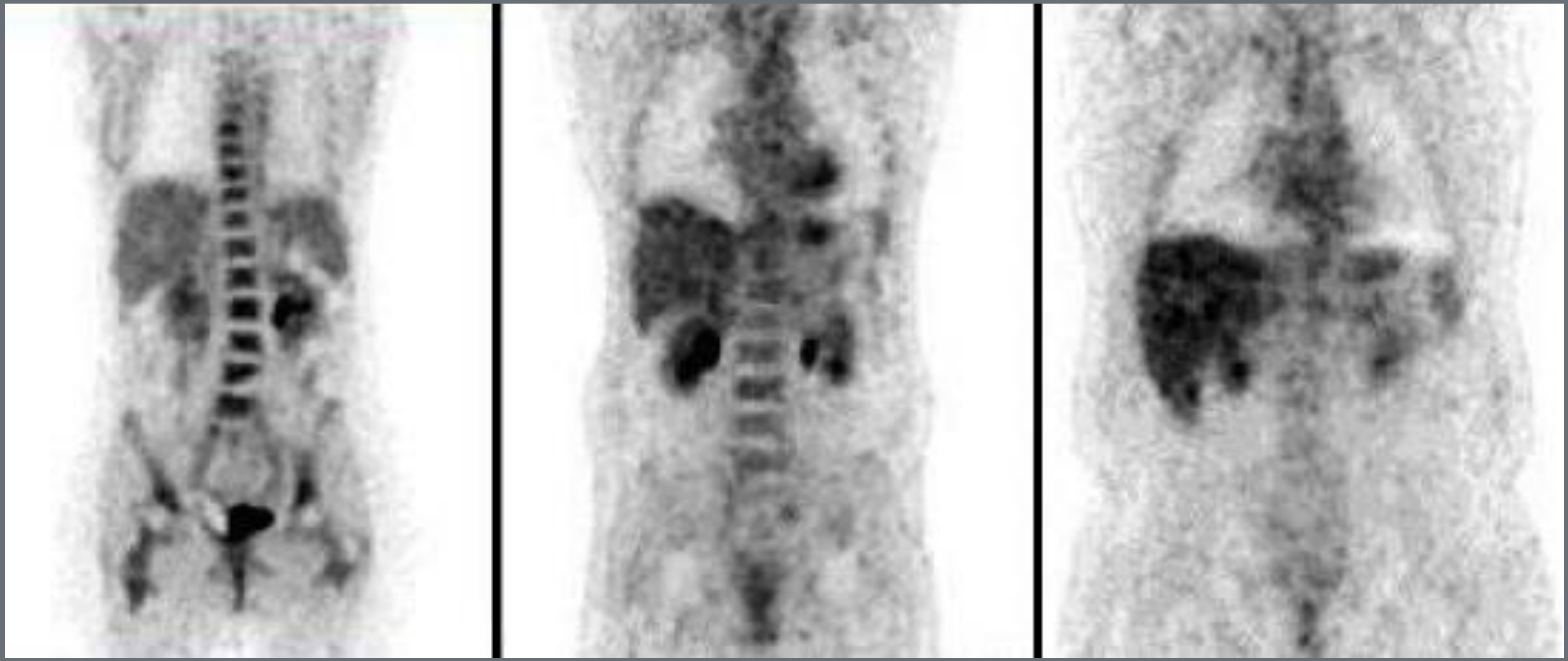
Analog Done w/ Discrete, Digital Done w/ FPGA

Depth-of-interaction (DOI) blurring



(from Siemens Medical)

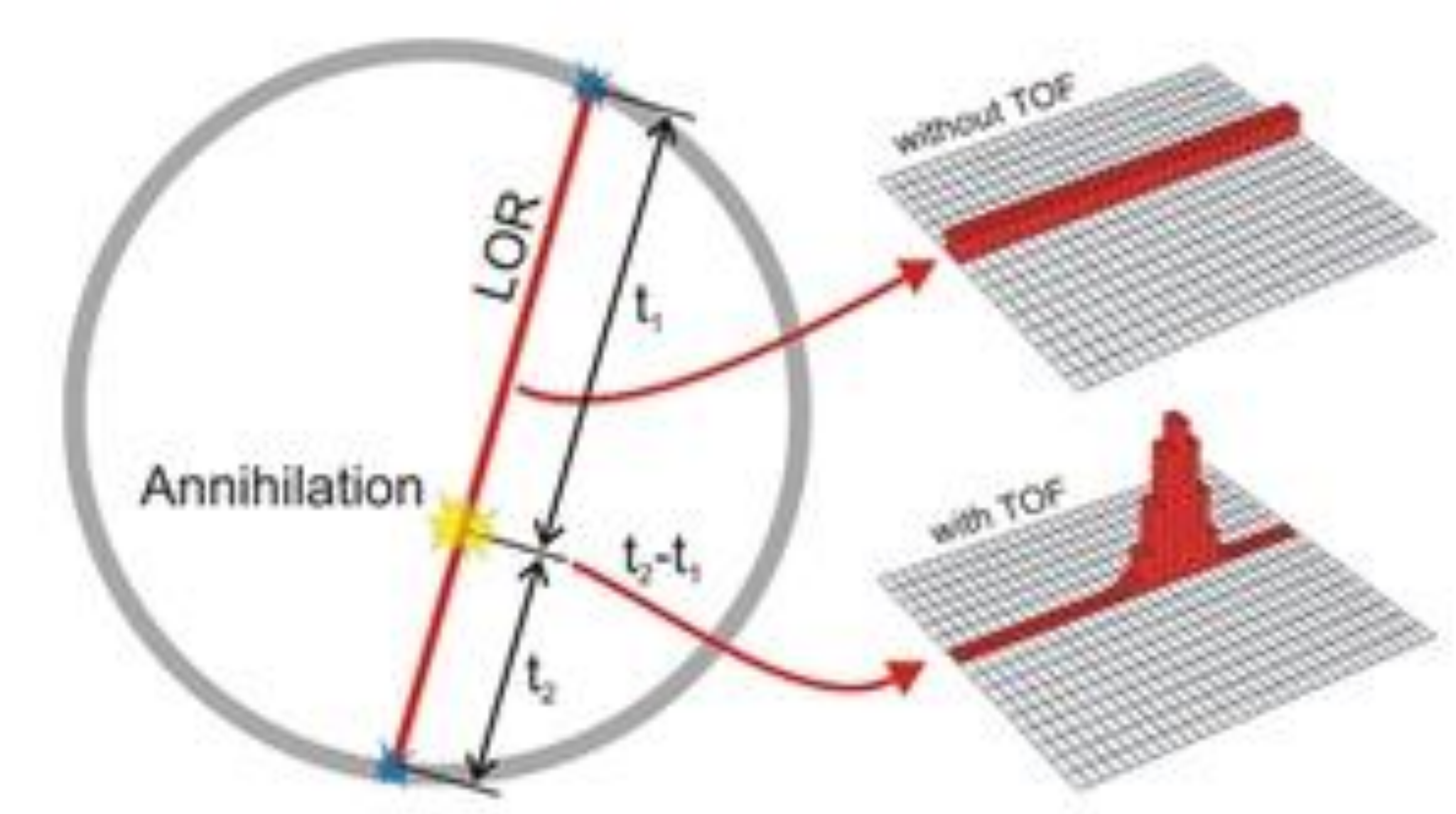
Large Patient Problem



58 kg 89 kg 127 kg

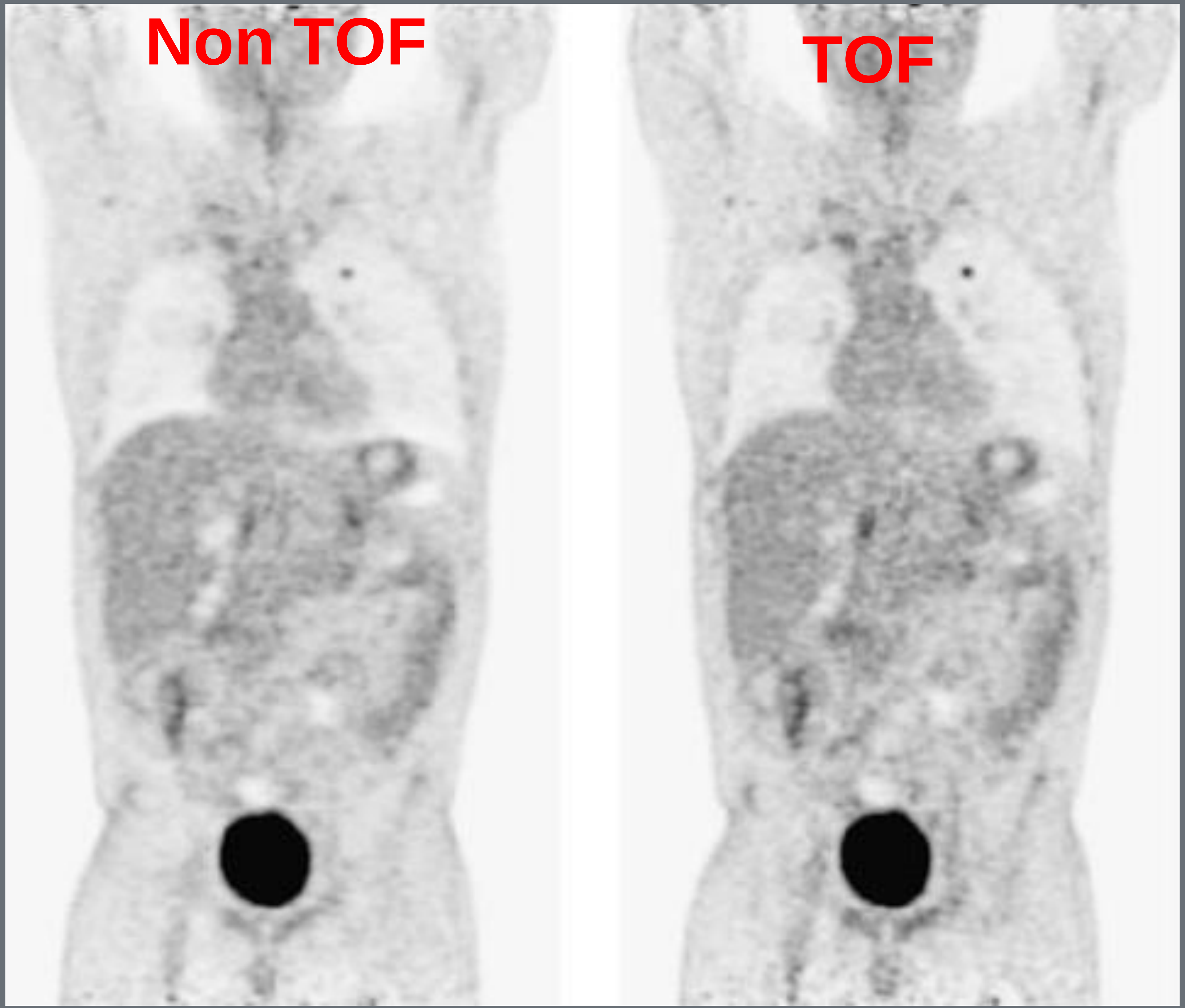
(J Karp *et al*)

Time-of-flight (TOF) PET



(http://flc.desy.de/pet/intro/index_eng.html)

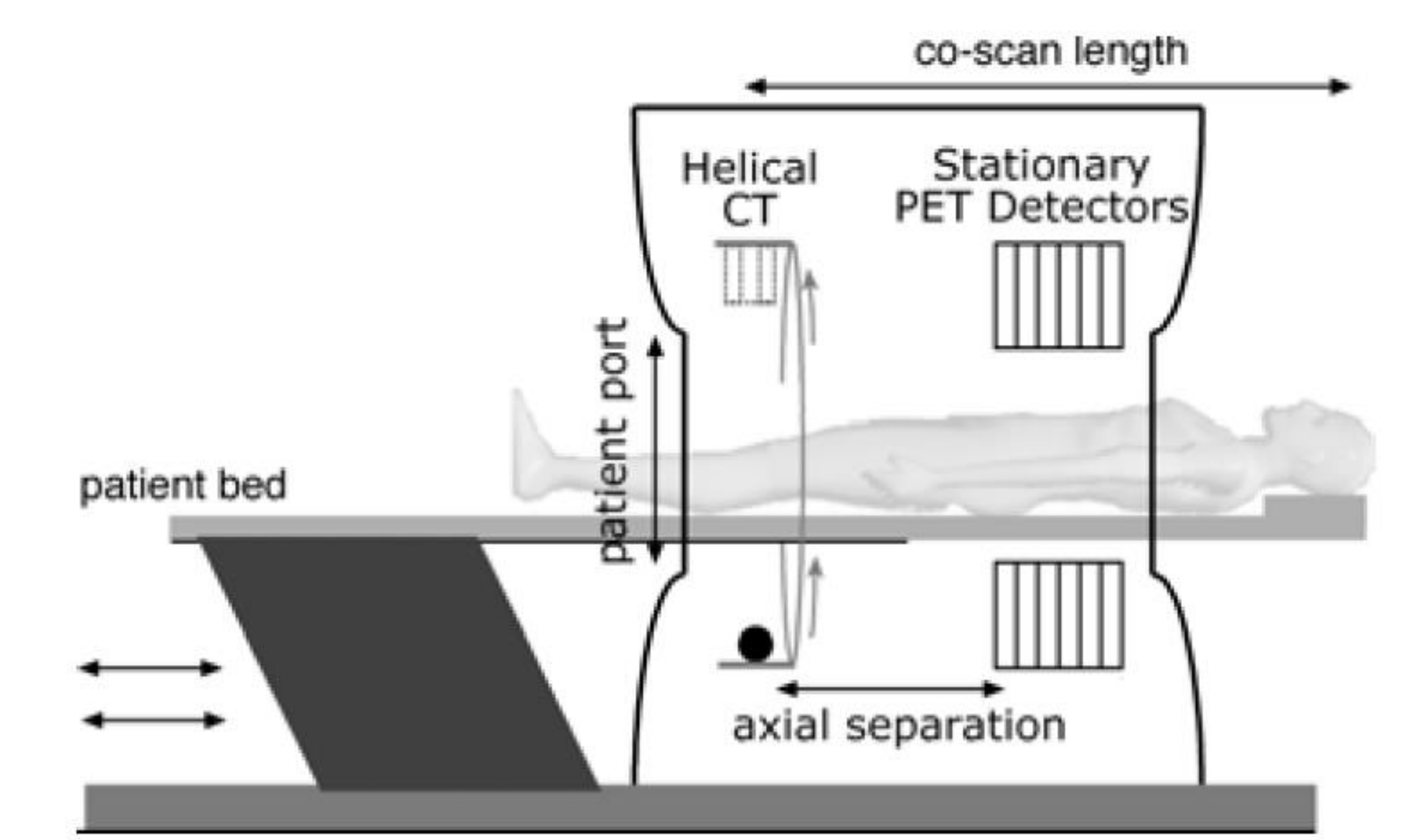
$$SNR_{TOF} = \sqrt{\frac{D}{\Delta x}} \cdot SNR_{non-TOF}$$



equal scan time

(M Conti, EJMMI Physics, 2011)

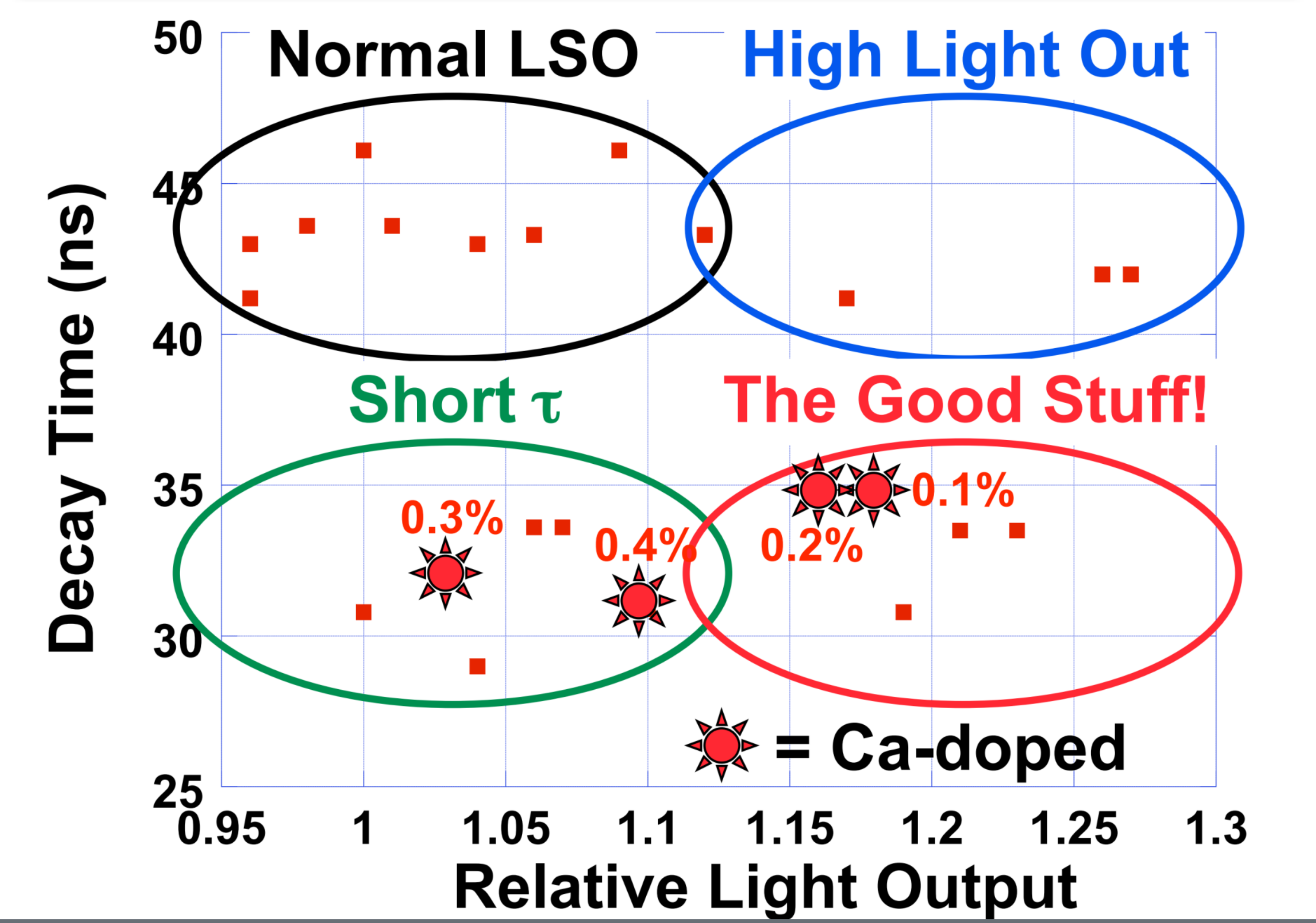
PET/CT

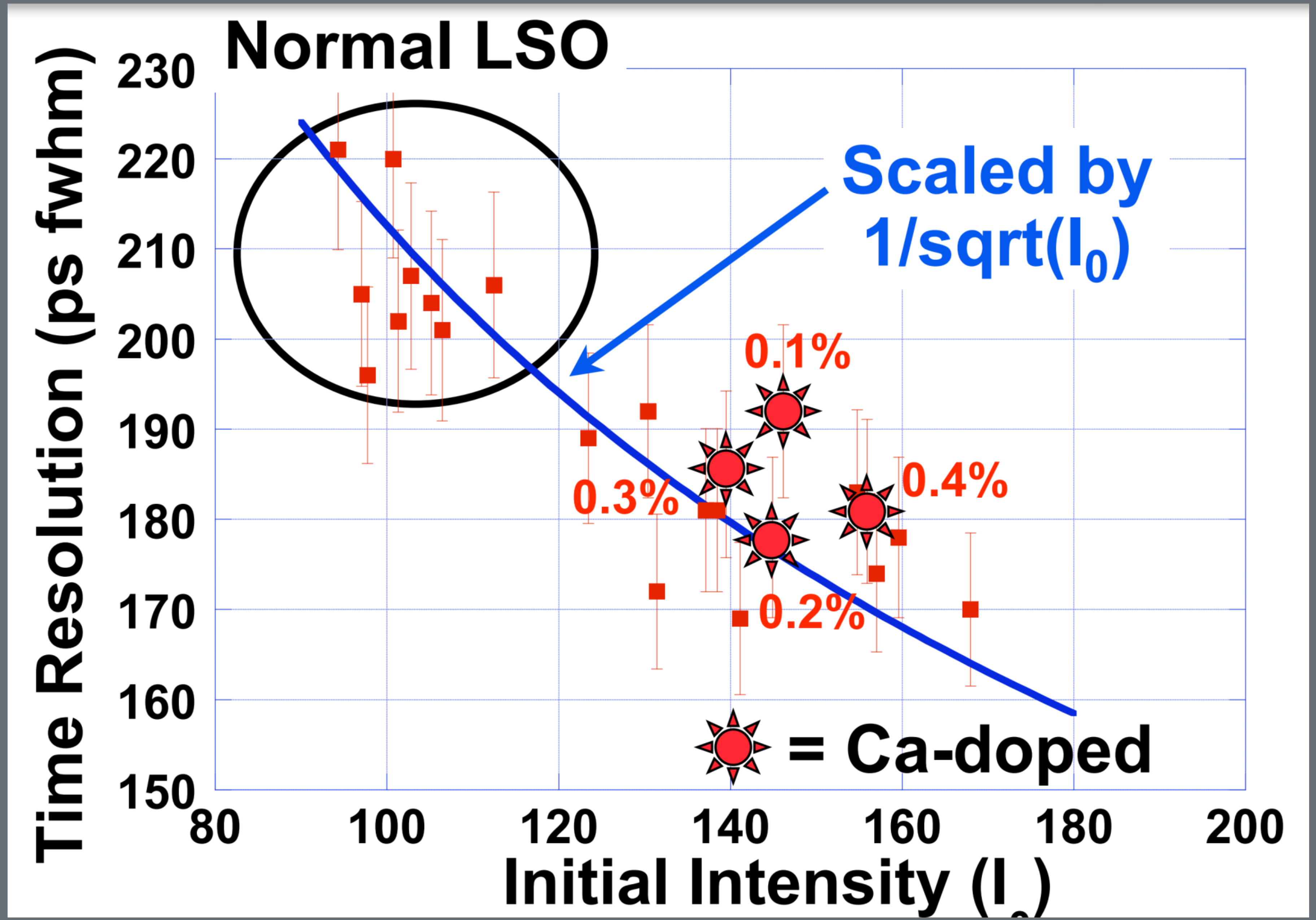


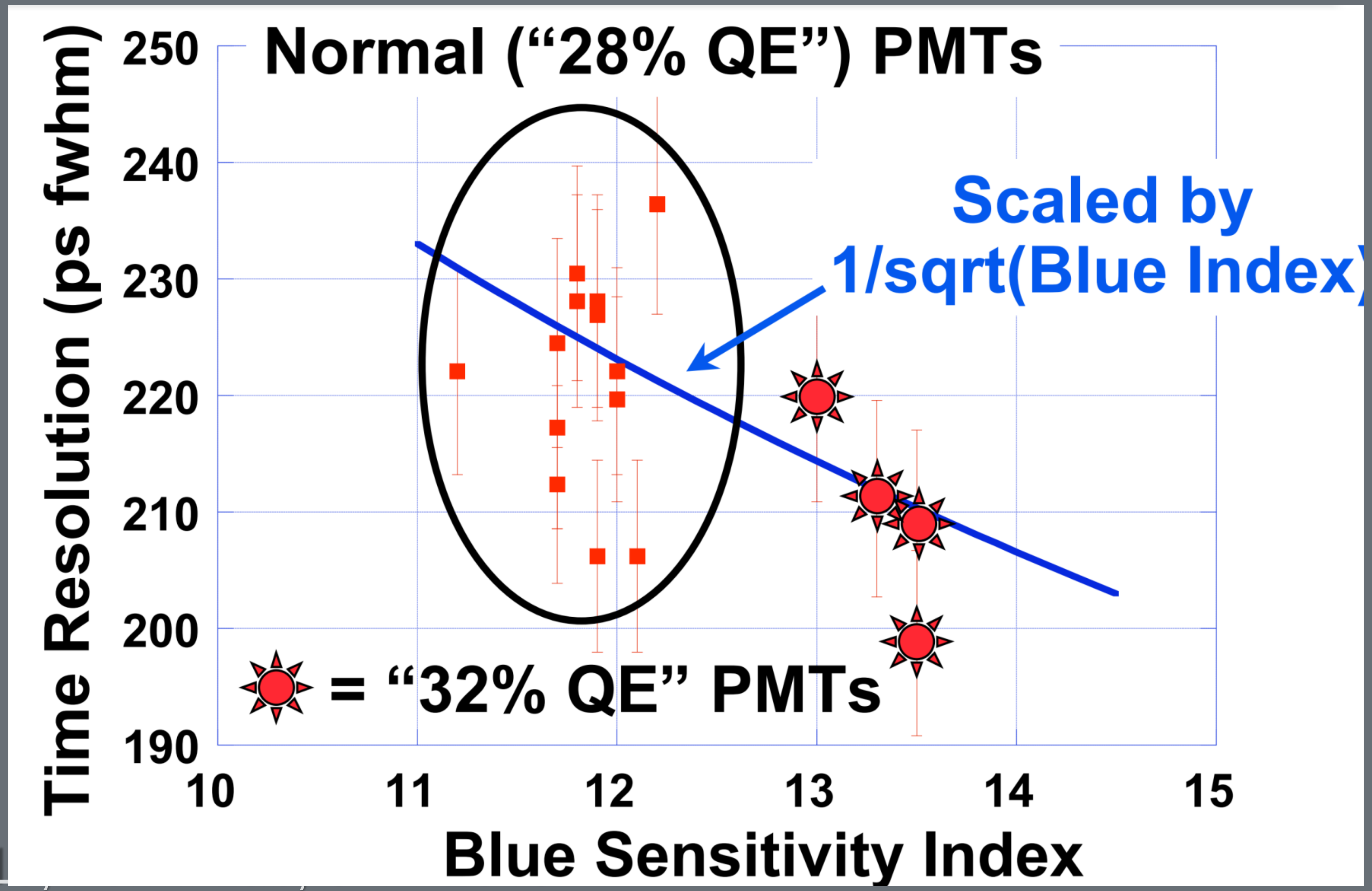
All 3 (couch, CT and PET) must be in accurate alignment

~500-600 ps with LYSO/PMT

Improve TOF resolution

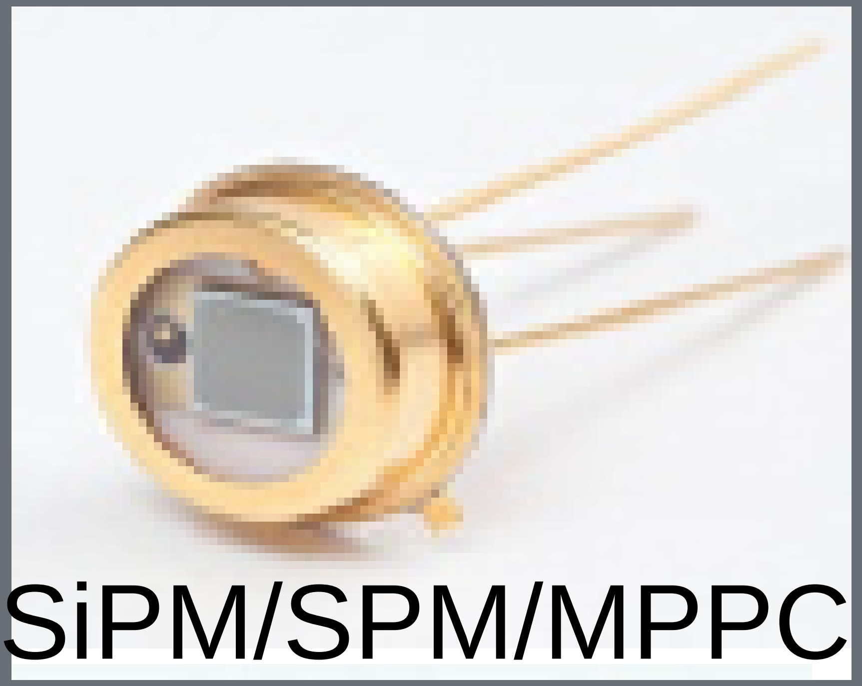


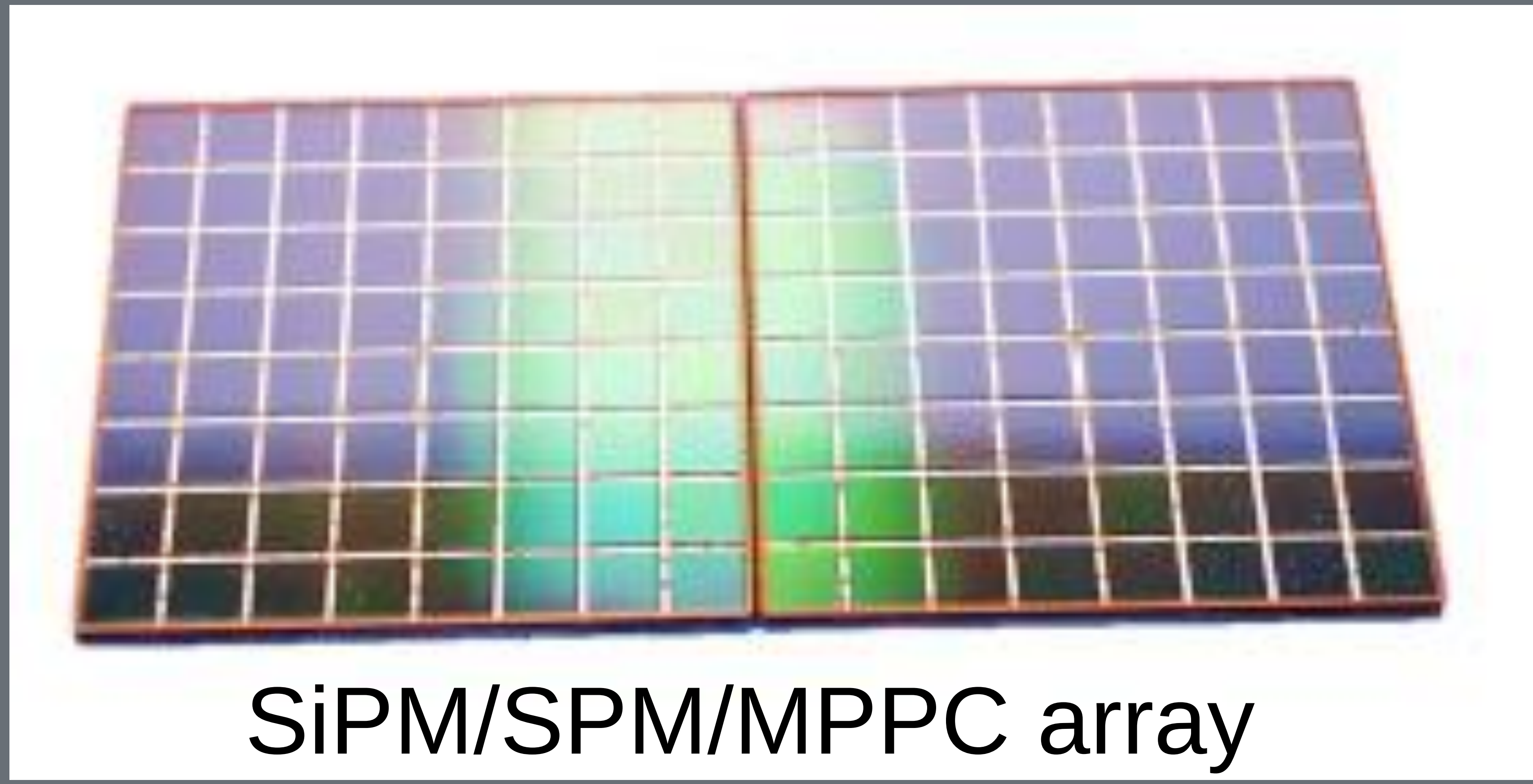




Silicon Photomultiplier (SiPM)

~1 inch, >1000 V, fragile, very sensitive to magnetic fields, TOF capable





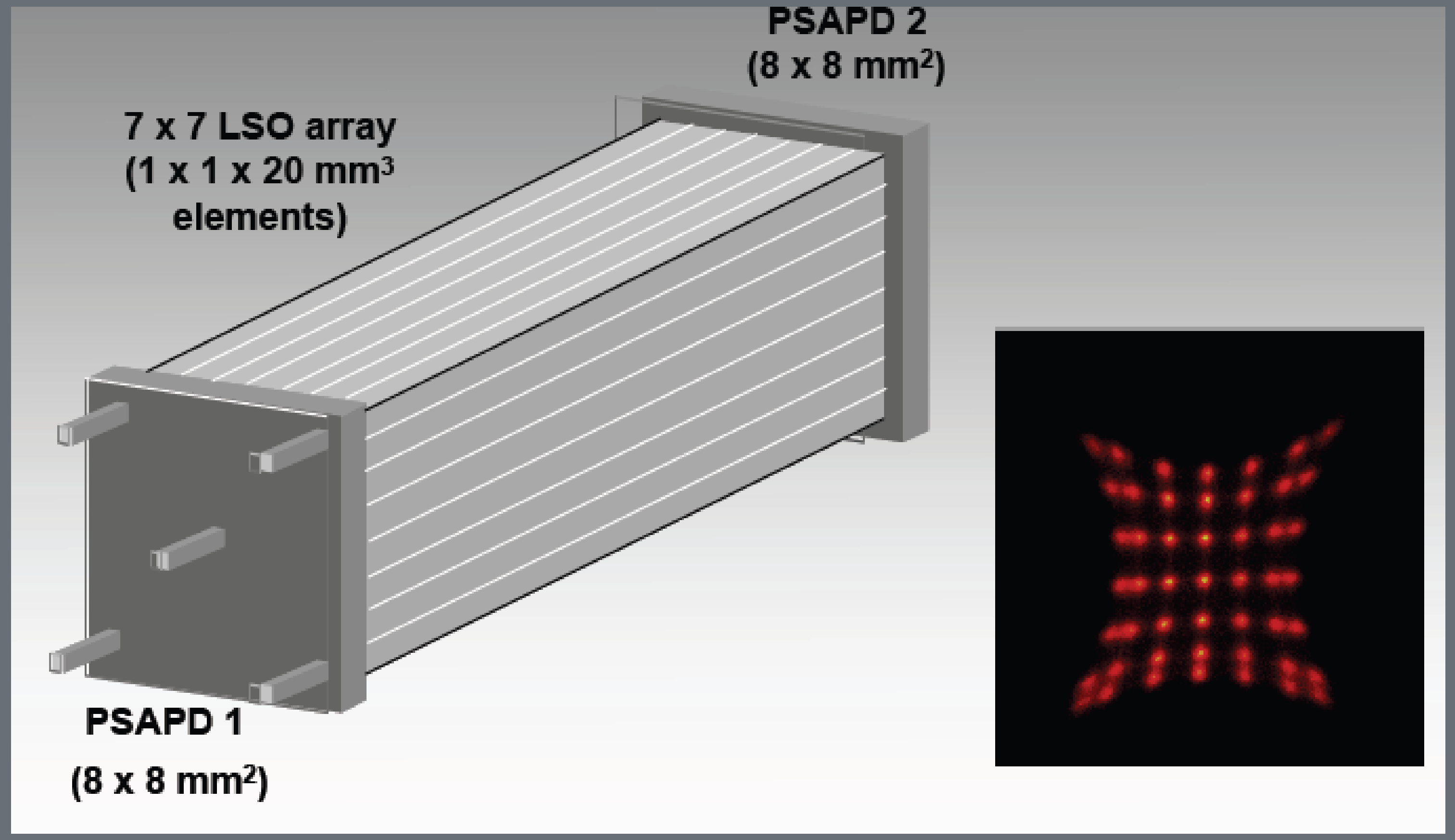
1-6 mm pixel, array format, 30-70 V, robust, MR compatible, TOF capable, low-cost potential

Pros and Cons of Silicon Photo Multipliers

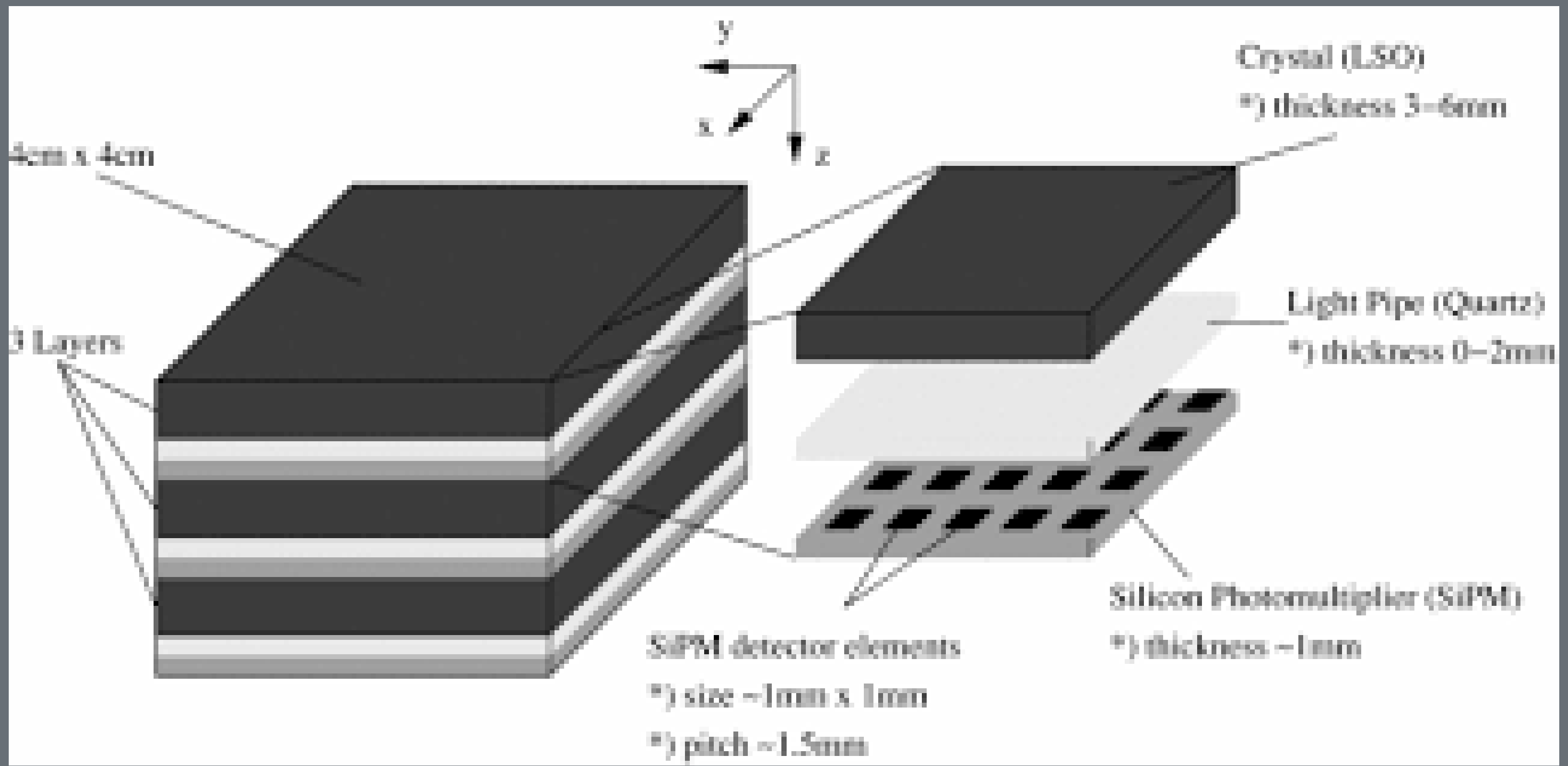
	PMT	APD	Si-PM
Amplification	10^6	10^2	10^6
Magnetic Field	Sensitive	Not sensitive	Not sensitive
Bias Voltage	1000V	350-2000V	20-70V
Signal / Noise Ratio	High	Low	High
Dynamic Range	High	High	Small
Timing Properties	< 1ns	2-4ns	<1ns
Electronic Readout	Voltage Amplifier	Charge sensitive pre-amplifier	Voltage Amplifier

Slide Courtesy: Armin Kolb, University of Tuebingen

Compact SiPM based PET detectors



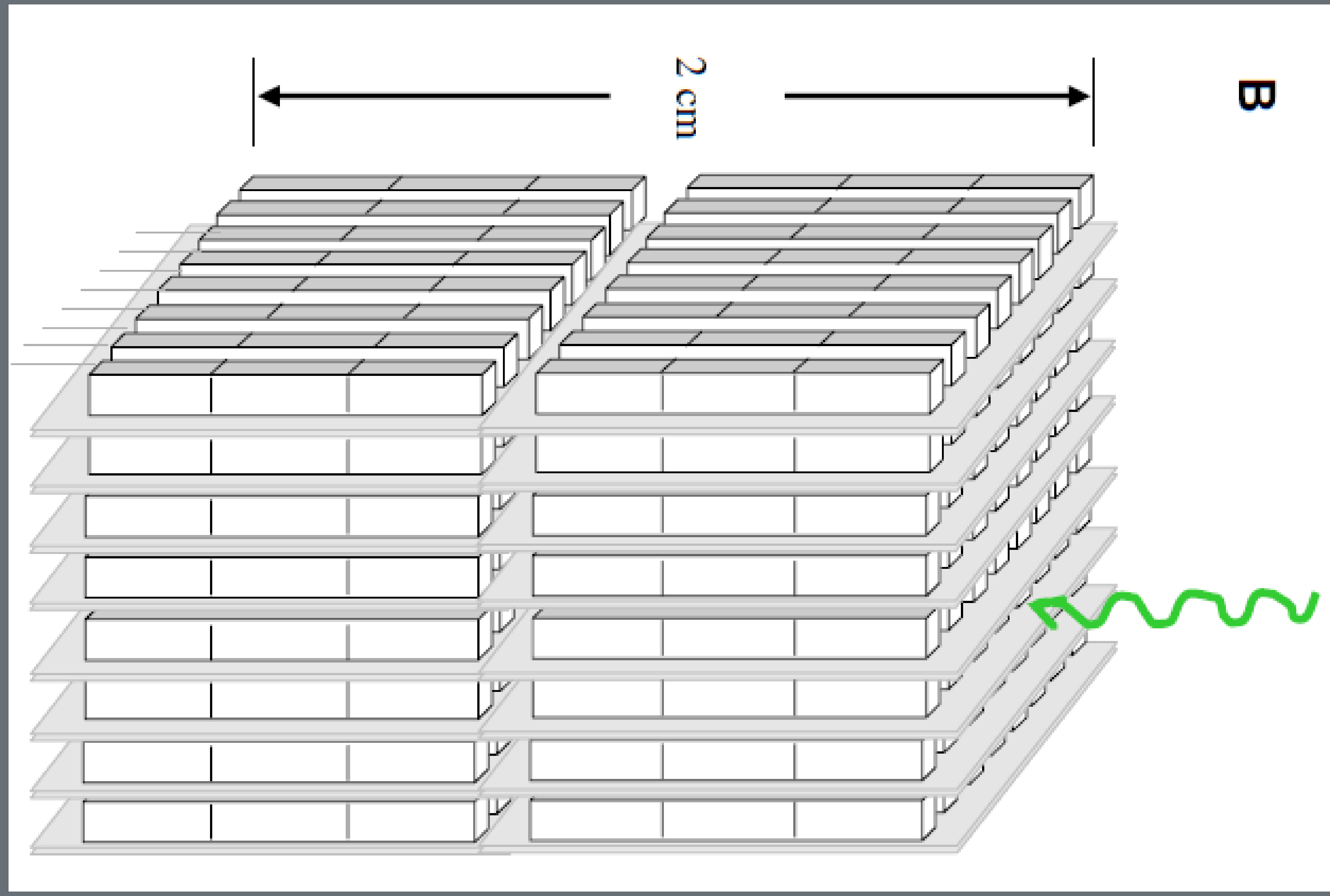
double-ended (SR Cherry *et al*)



Multi layered (A. Del Guerra *et al*)

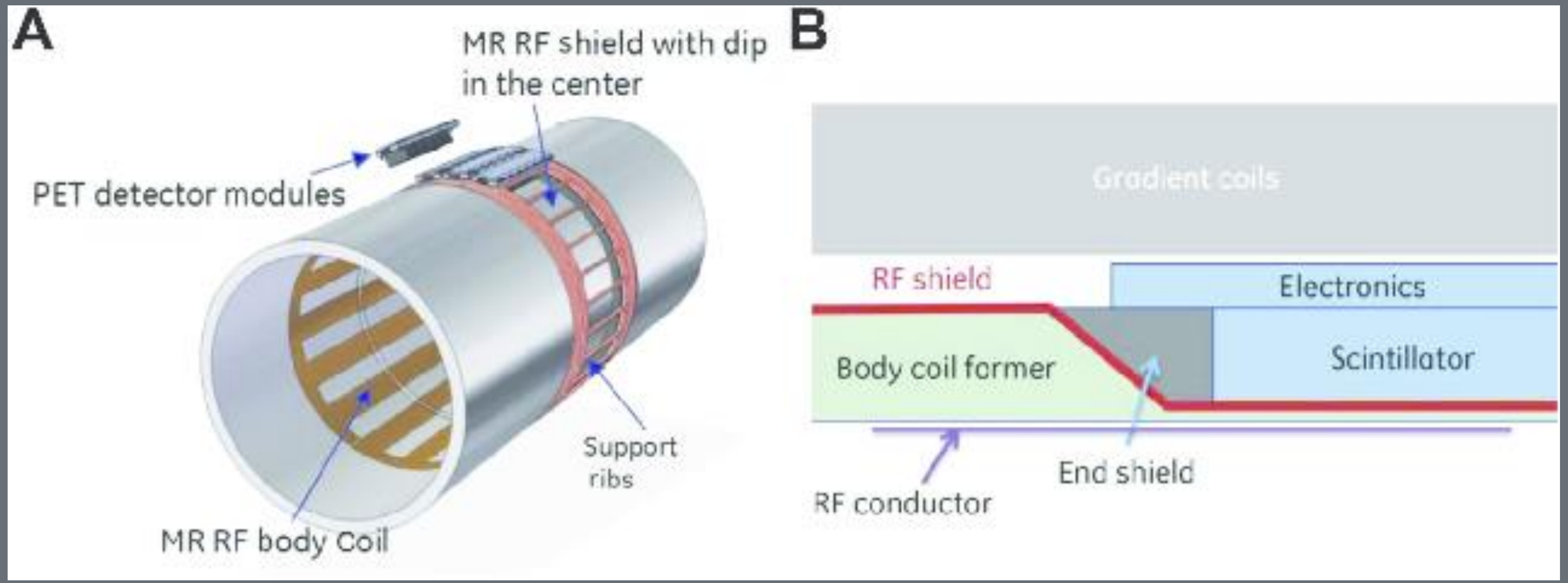
Side readout

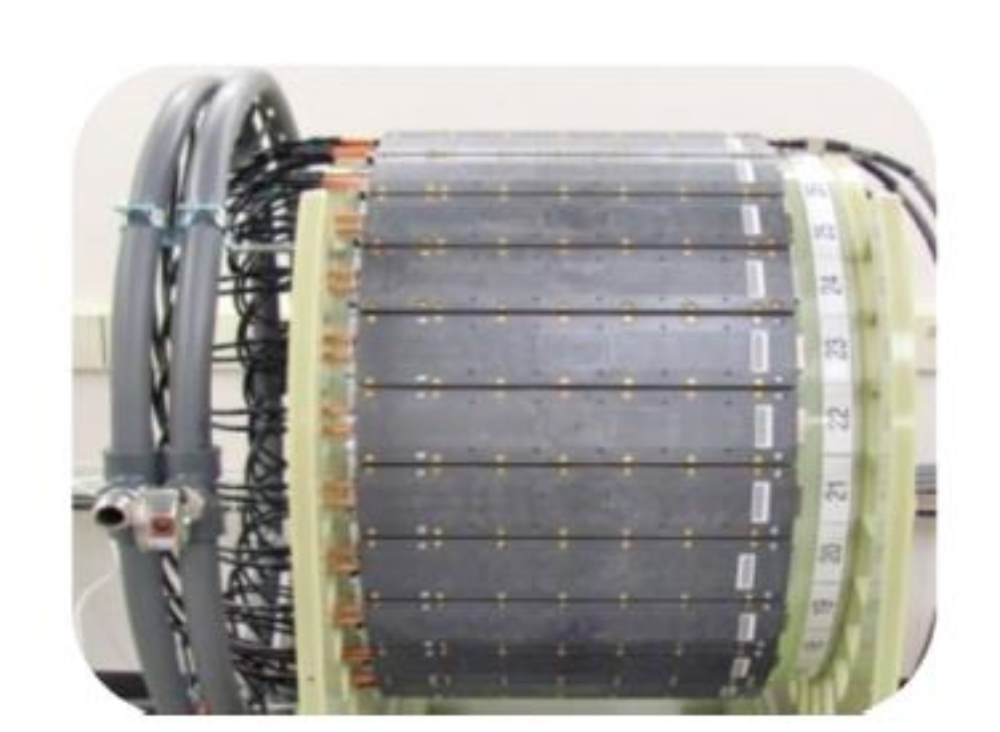
(CS Levin *et al*)

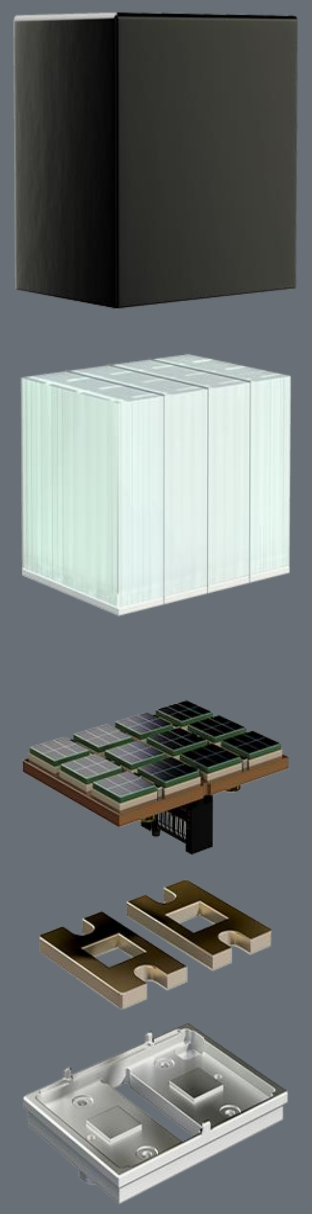


Can support TOF also

PET/MR







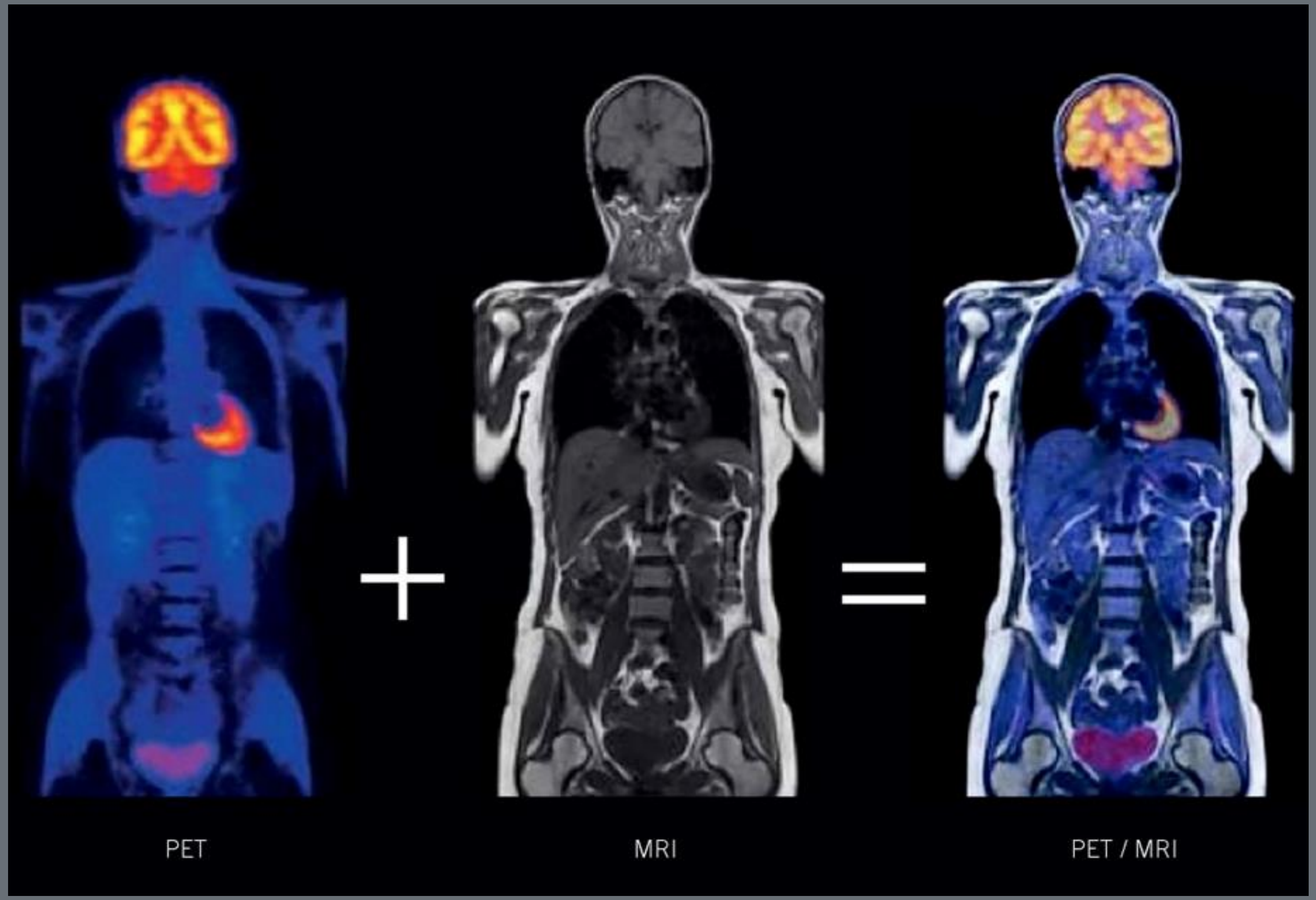
Light Tight RF Shield with copper coating

LBS array with (ESR)

SiPM with circuit boards/ASICS

Thermal coupling

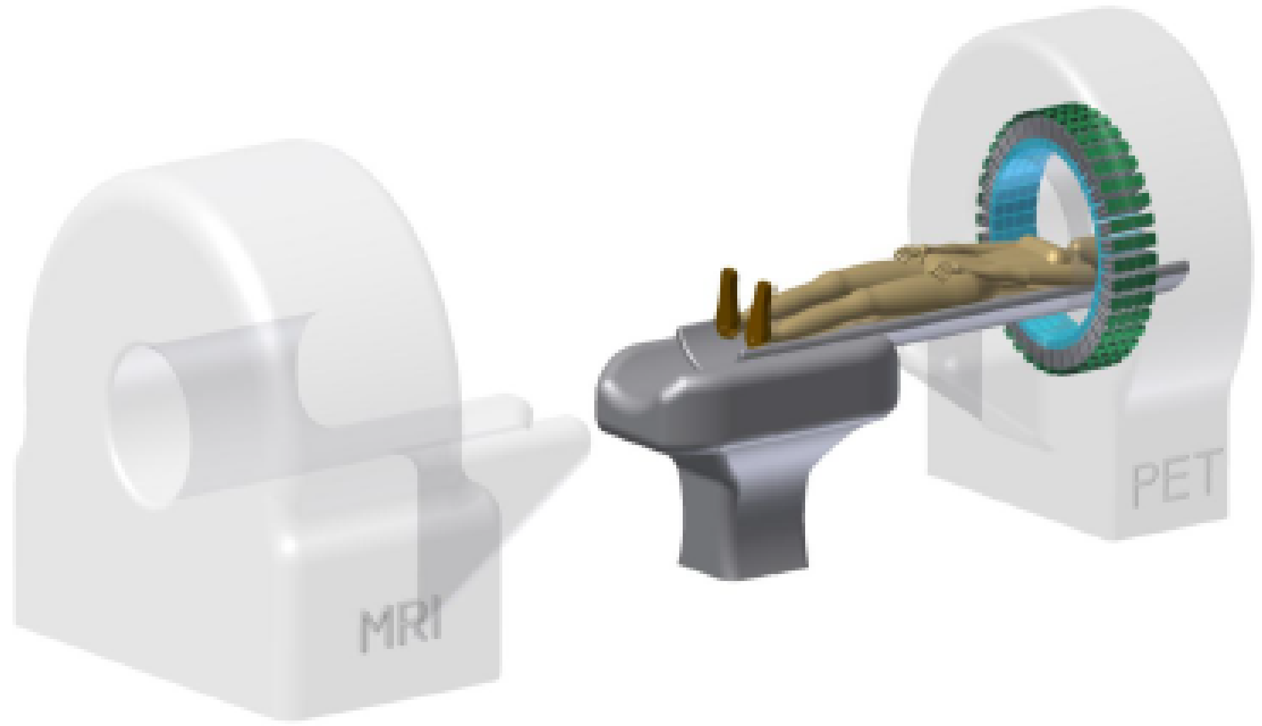
Aluminum mounting



25 cm AFOV
10.5% ER
390 ps CRT

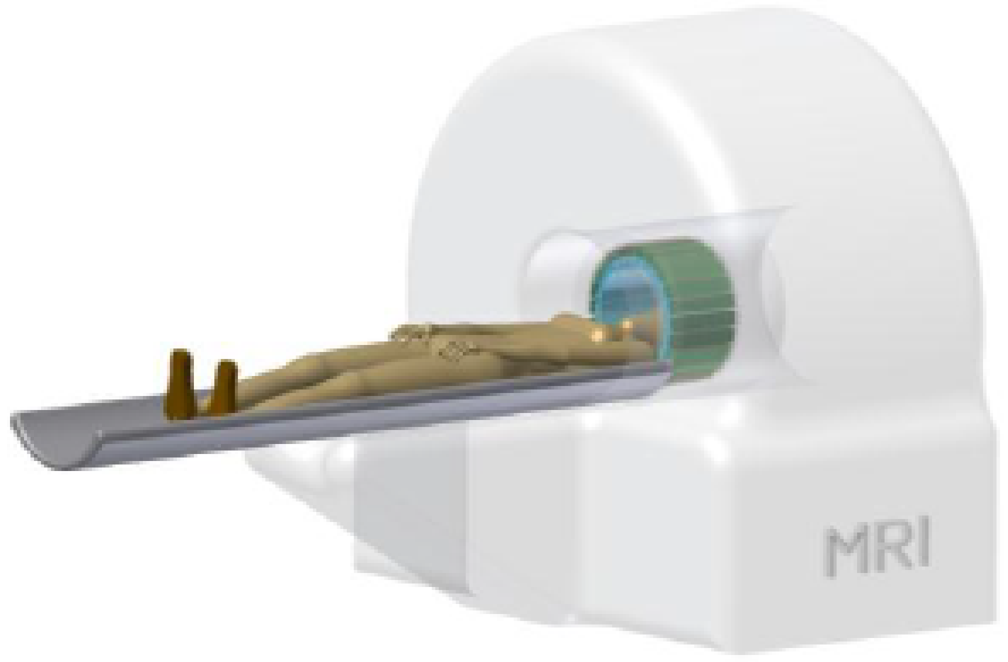
Design Approaches

side-by-side



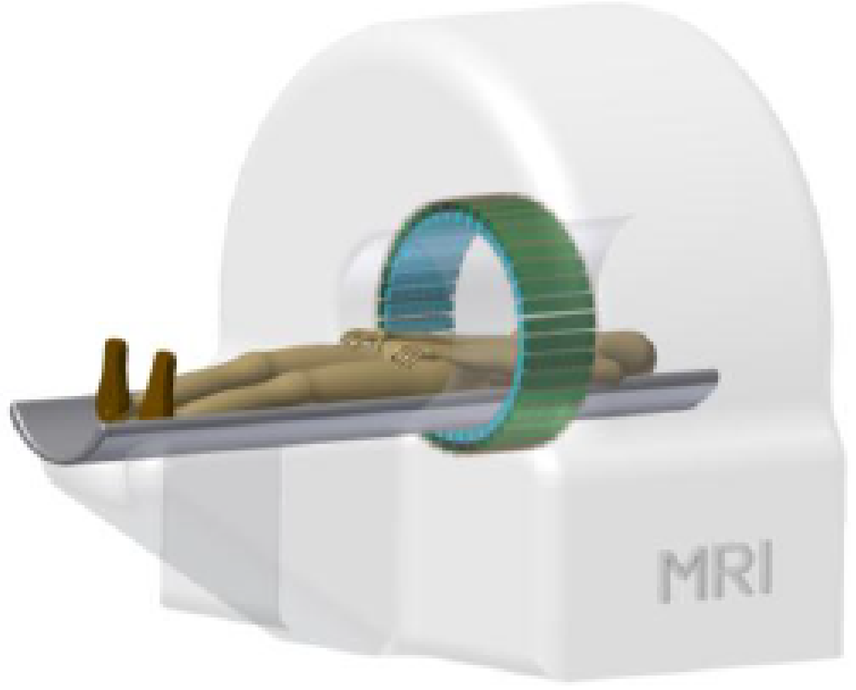
- Use current PMT technology
- Move PET readout away from MR field

PET-insert



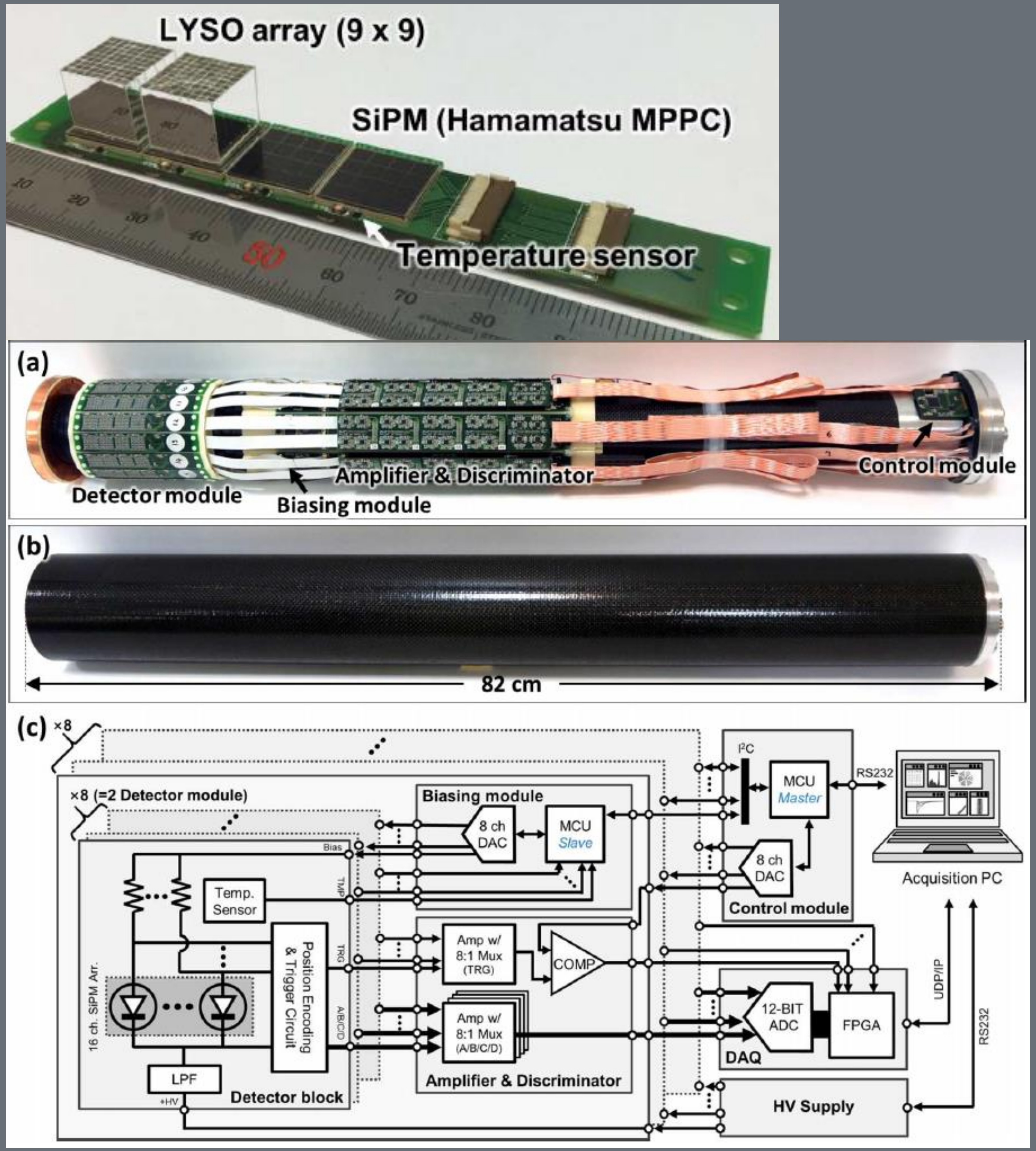
- Requires use of MR compatible light detector
- Only modify PET to be transparent to MRI

Integrated PET/MRI



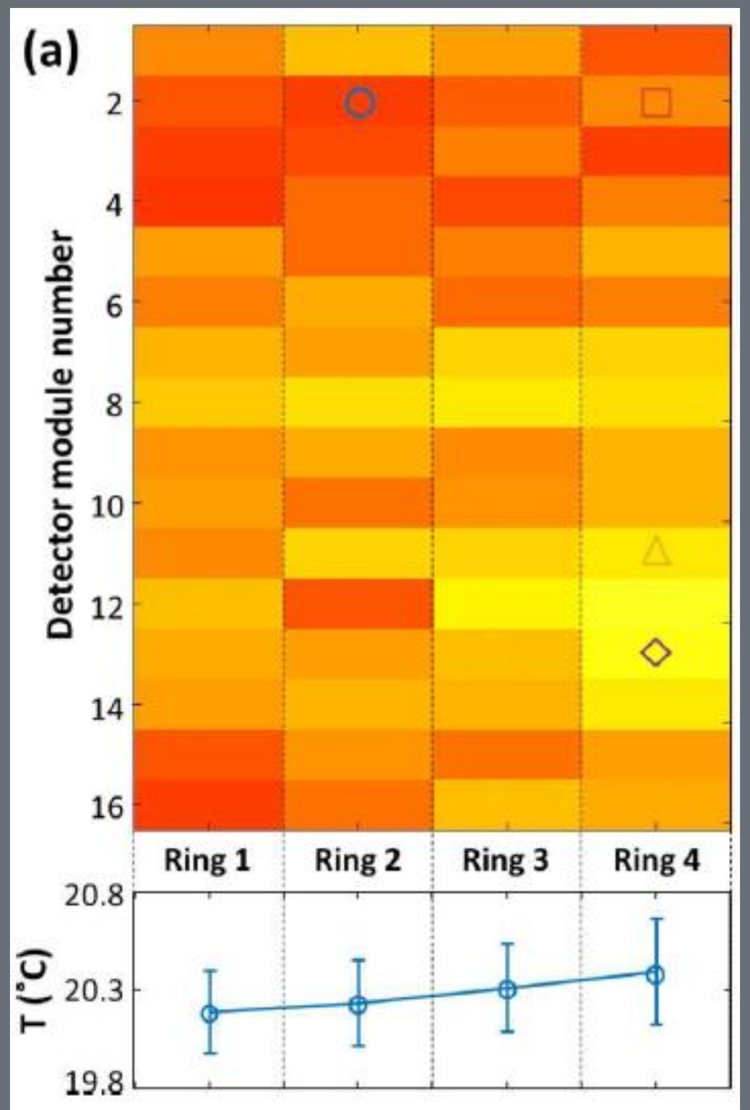
- Merge PET and MRI technology
- Fully integrate PET into the MRI hardware

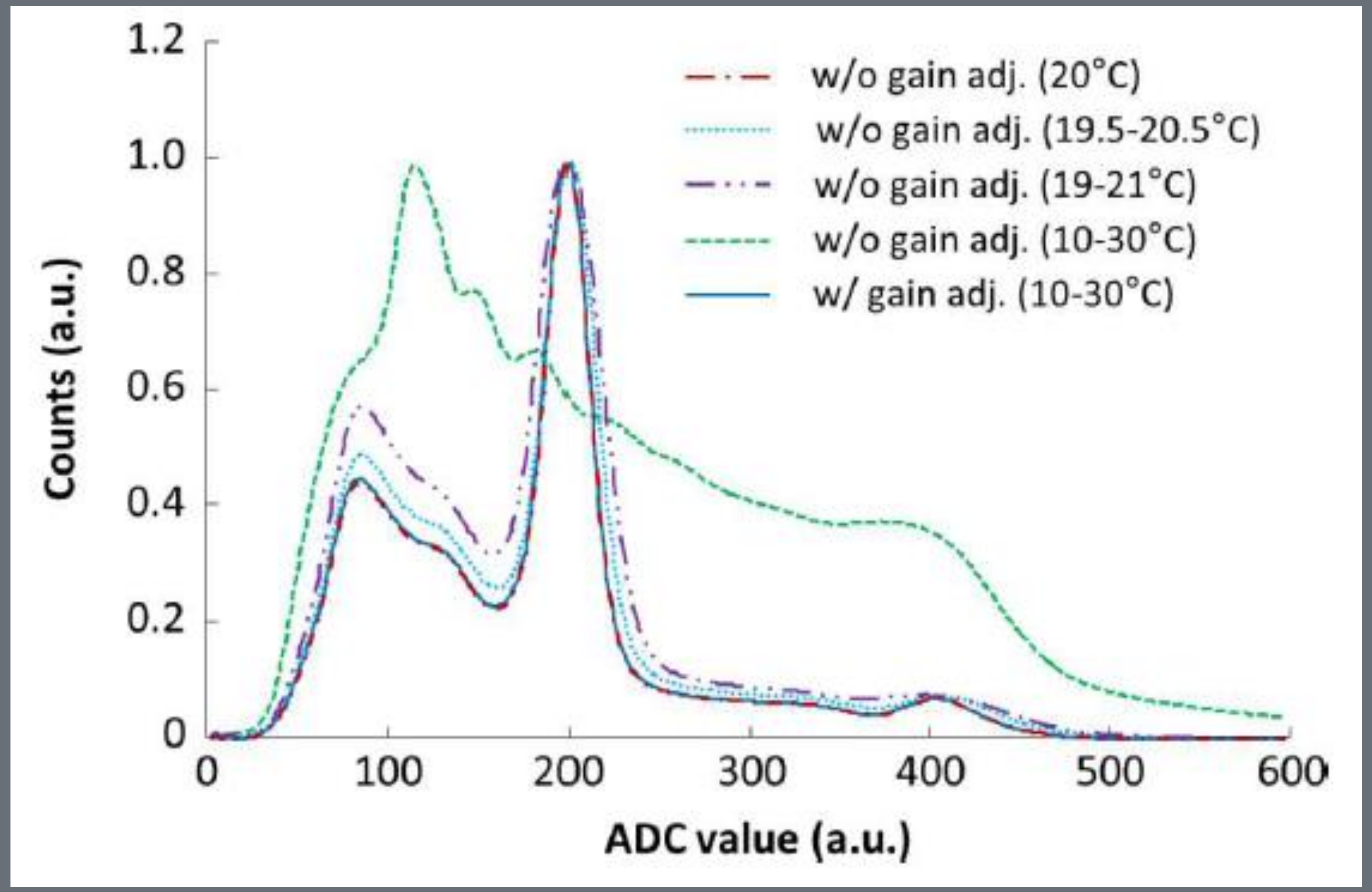
SiPM Based Inserts



(GB Ko et al, Med Phys 2015)

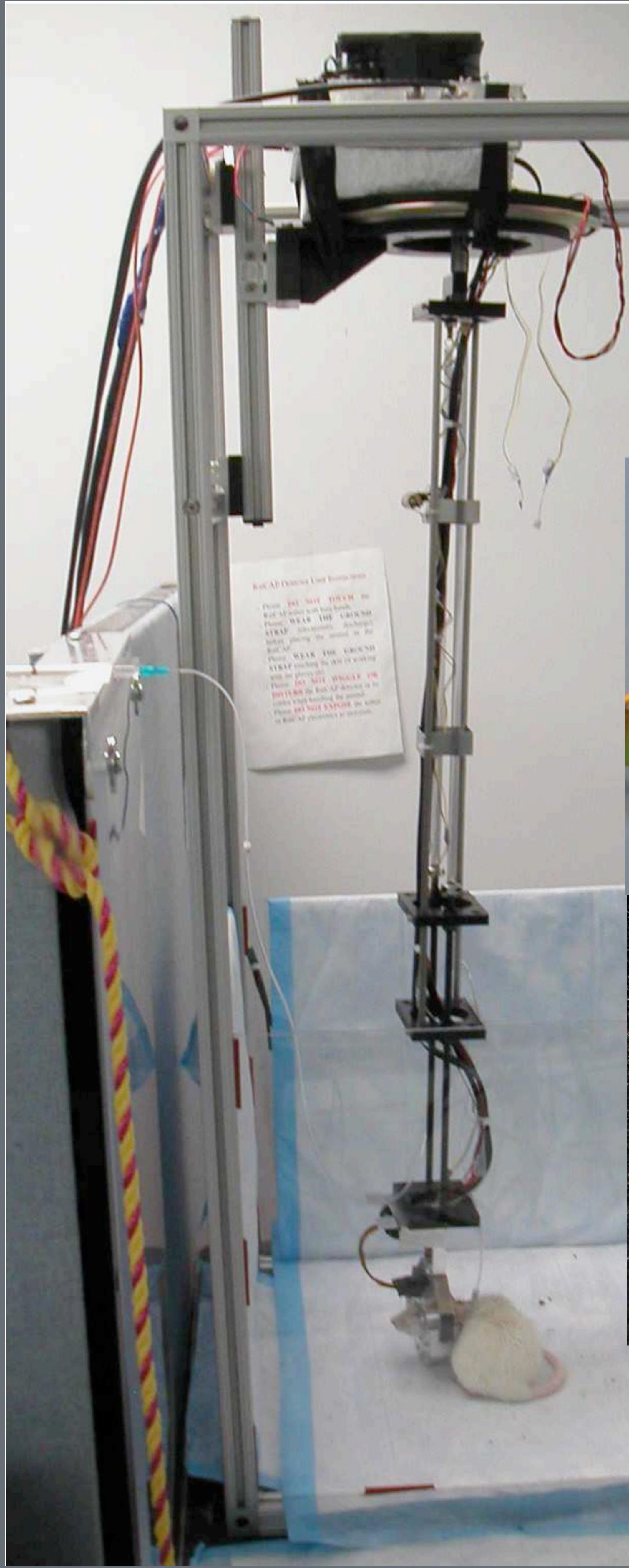
- 16 detector modules
- Axial FOV = 55m, ring diameter = 64mm
- Carbon fiber tube for shielding
- ID/OD: 60mm/100mm
- 1.2x1.2x10mm LYSO, 9x9 arrays, pitch 1.28mm
- 4x4 Hamamatsu SiPM array
- Resistor charge network reduces output to 4
- Resolution (OSEM/FBP): 0.75/1.31mm at center, 1.46/2.18mm at 14mm off center
- CRT ~ 1.33 ns
- Temperature and voltage controls

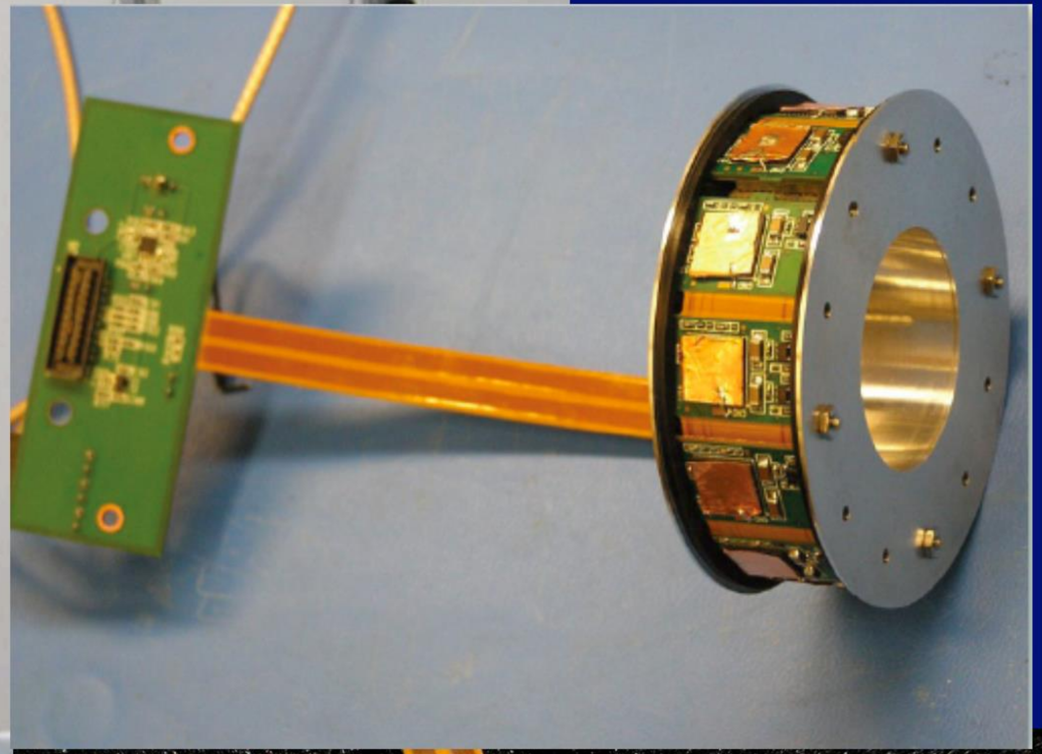


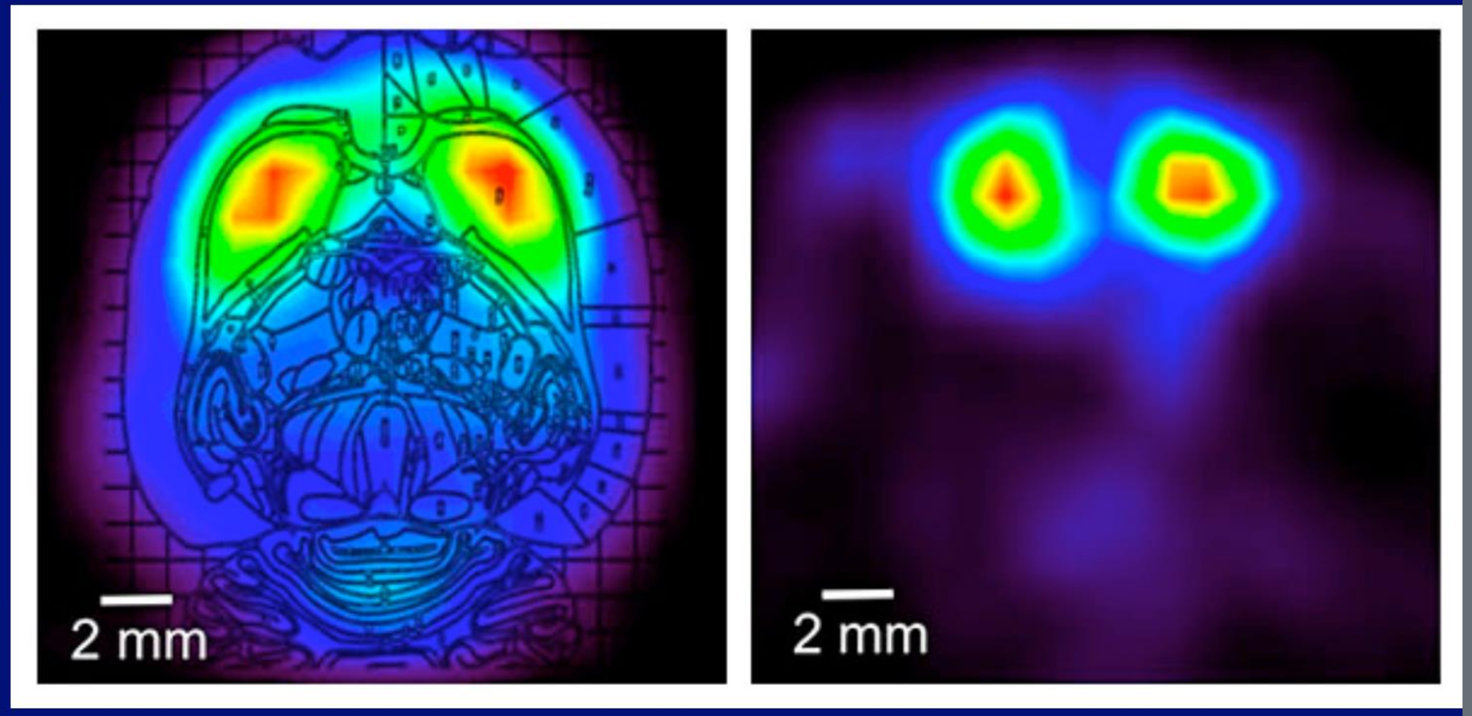


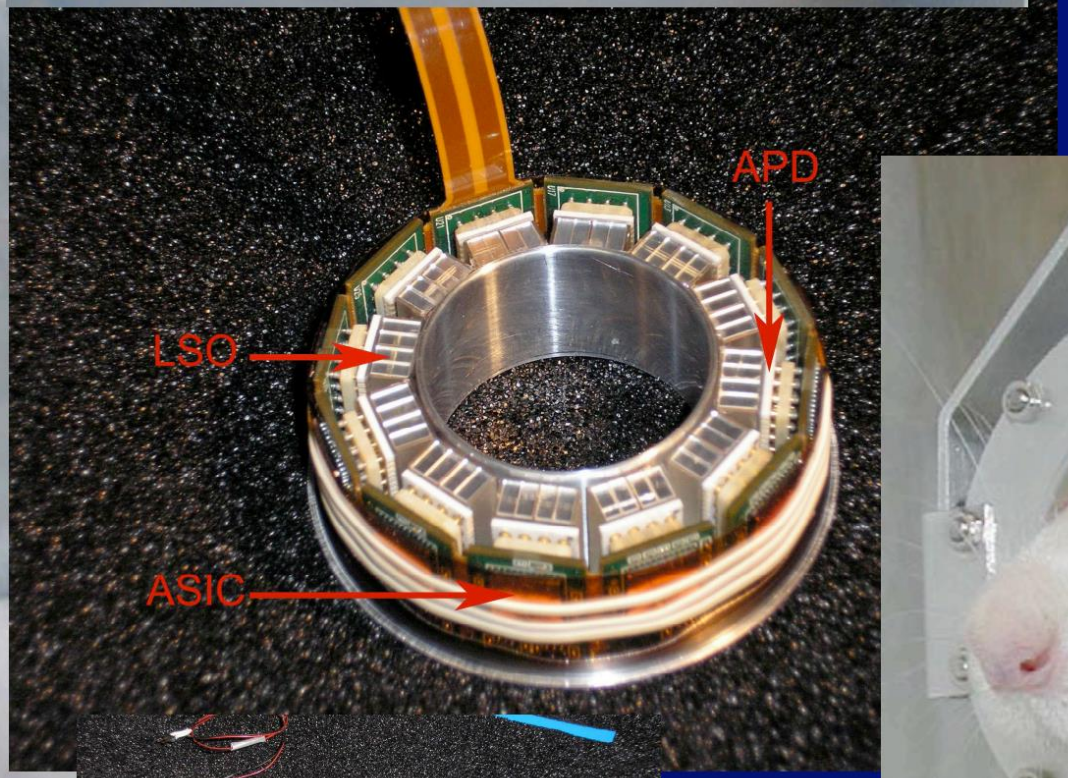
RatCAP for PET Imaging of Awake Animals

LSO + APD SiPM





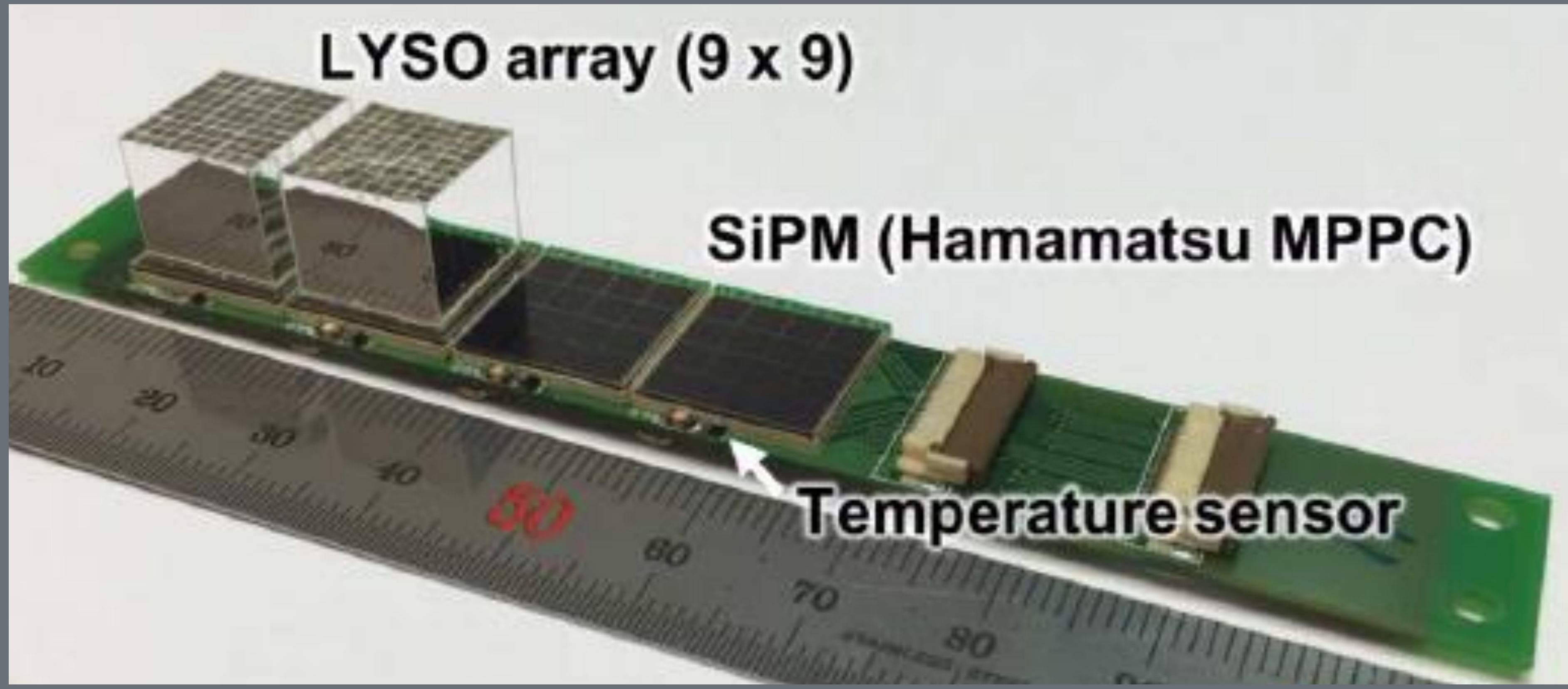


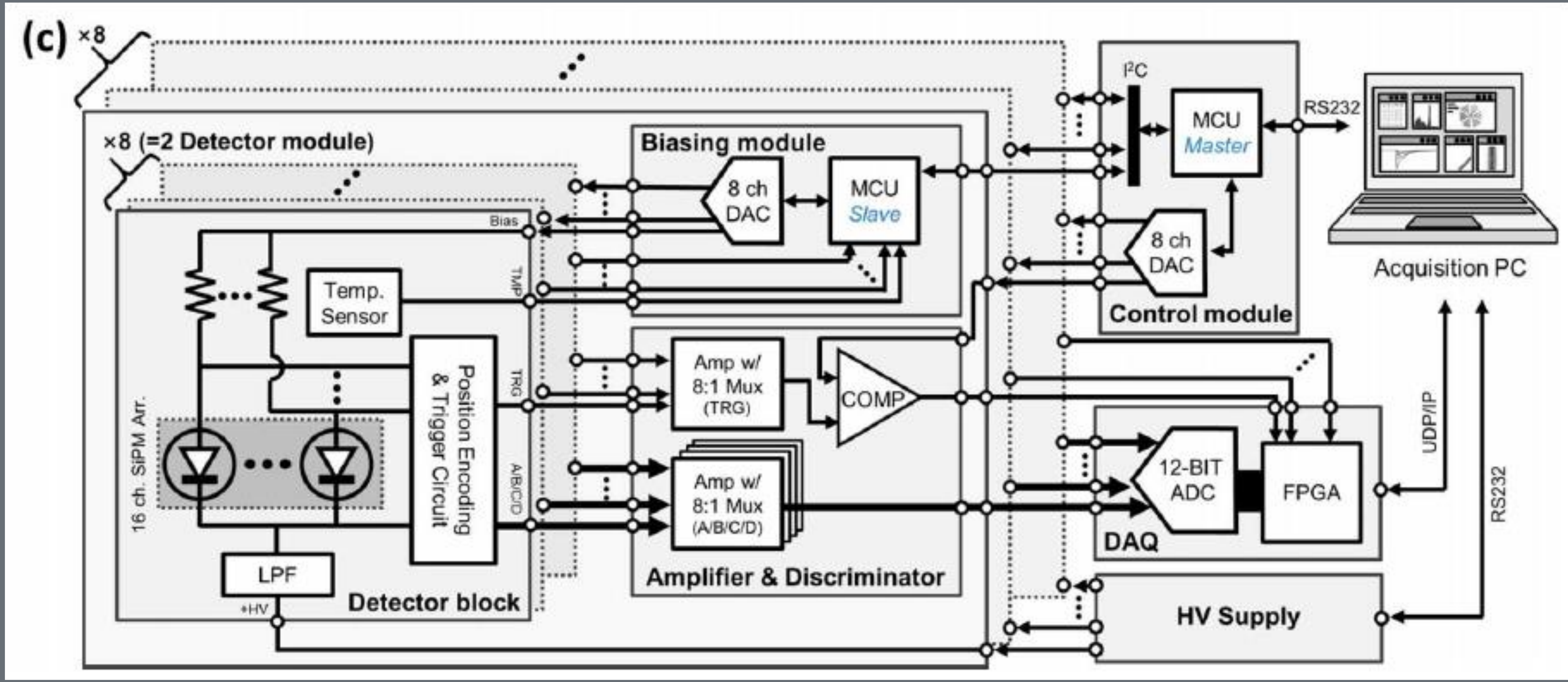


BROOKHAVEN NATIONAL LABORATORY

SiPM Based Inserts

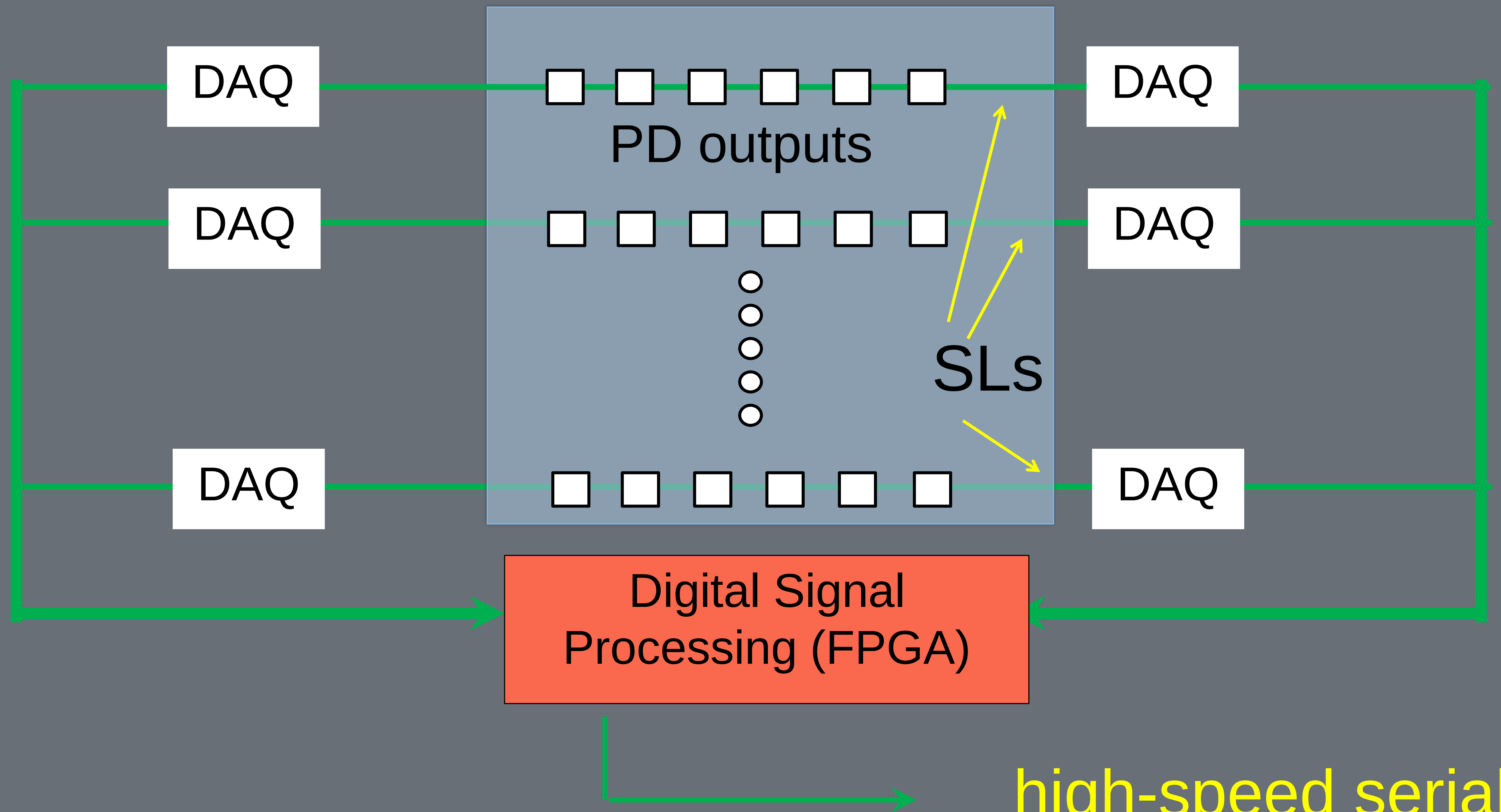
- 1.2x1.2x10mm LYSO, 9x9 arrays, pitch 1.28mm
- 4x4 Hamamatsu SiPM array
- Resistor charge network reduces output to 4



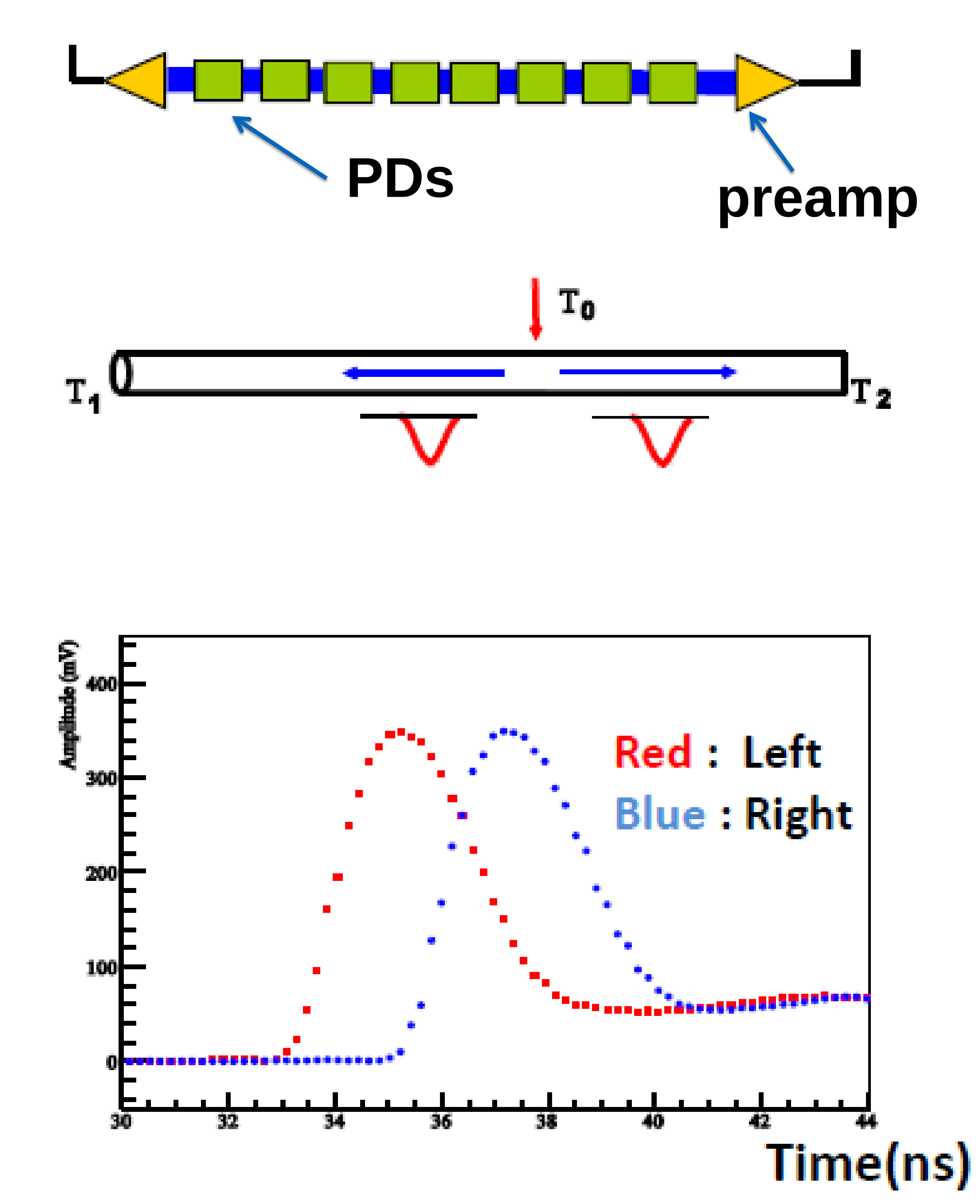


(GB Ko et al, Med Phys 2015)

Stripline (delay-line) Readout



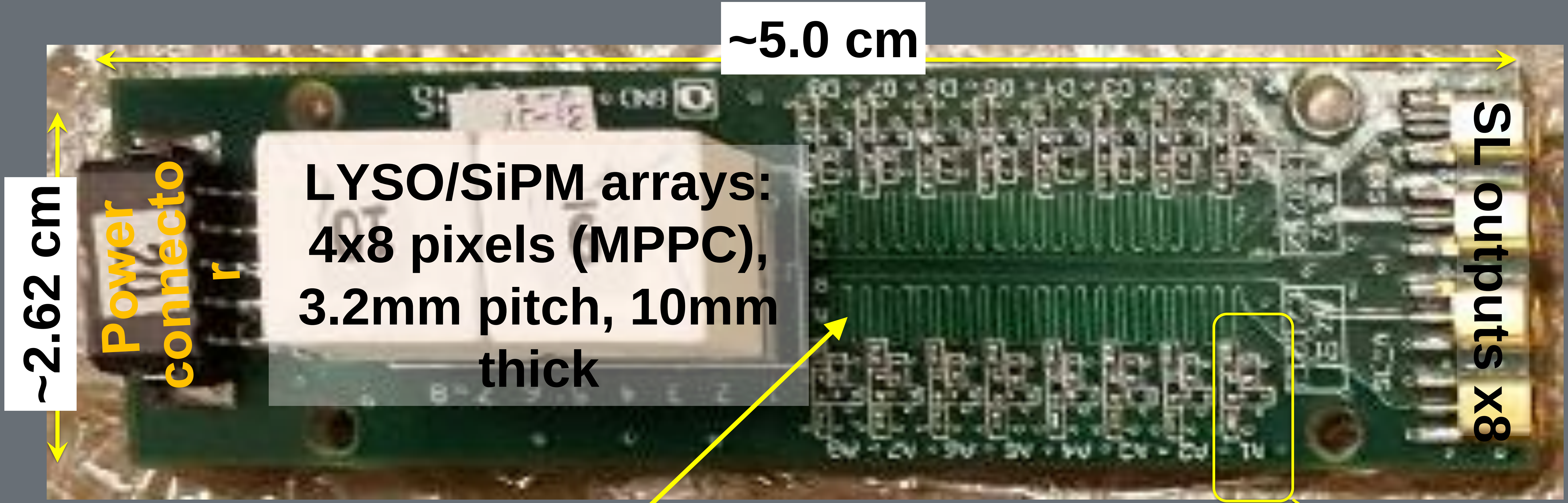
high-speed serial output



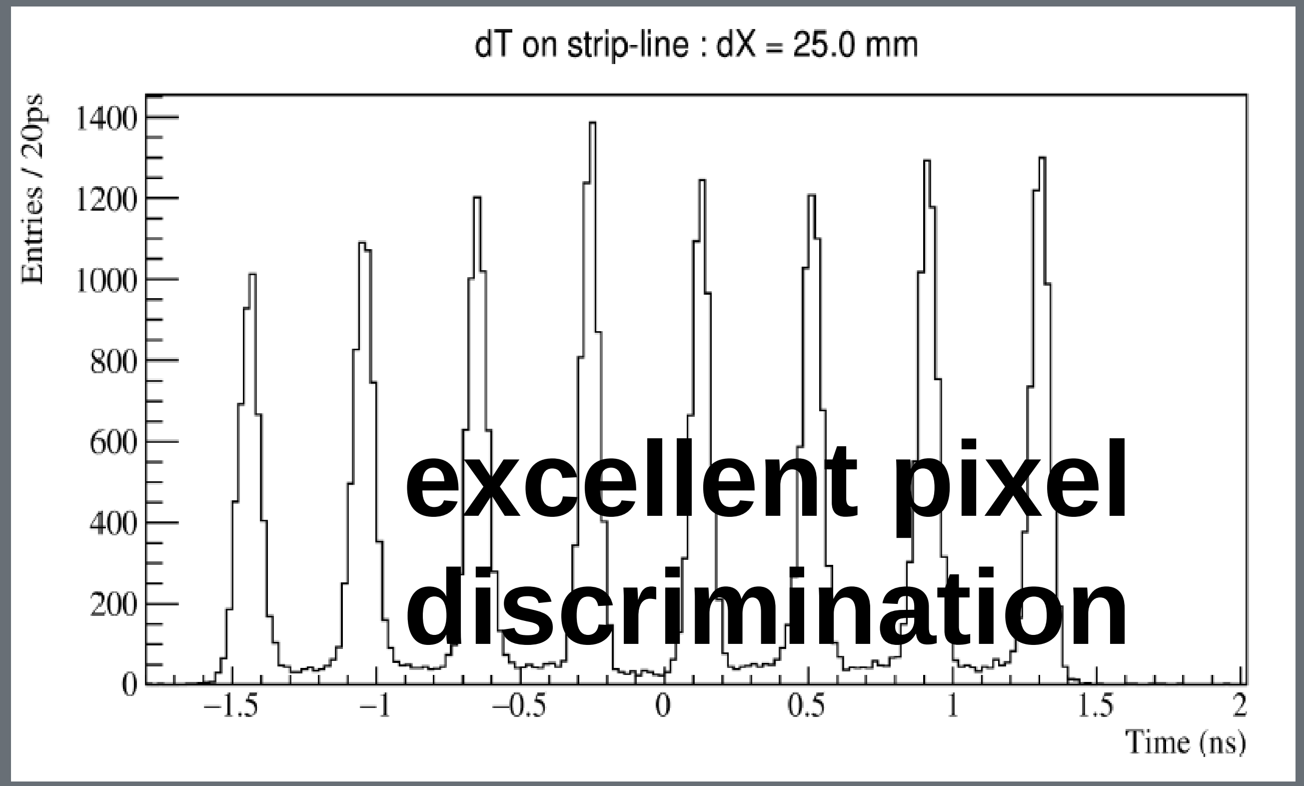
Waveform sampled at the two ends.

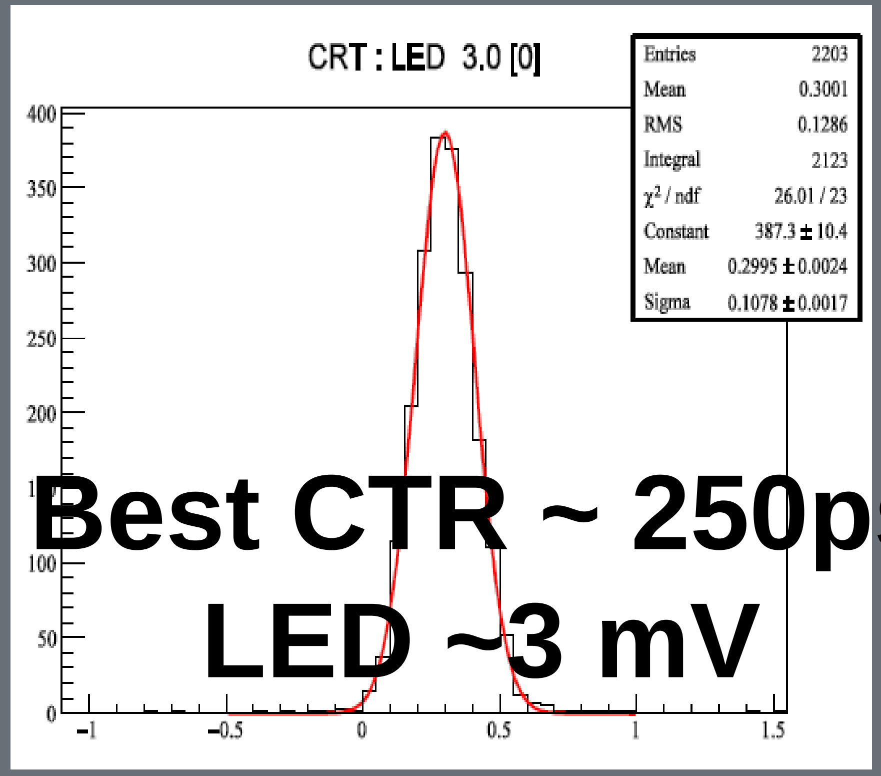
The position of firing PD is determined using the propagation time difference.

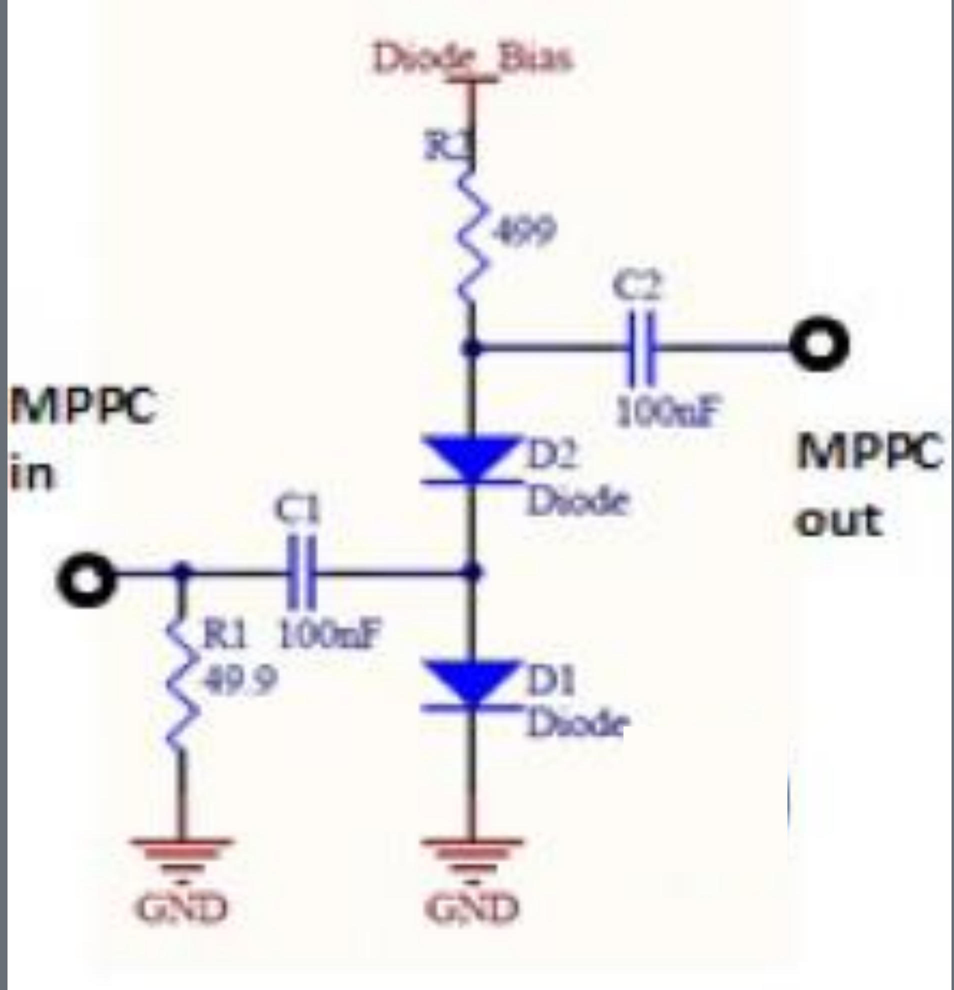
UChicago detector module



curvy SLs to increase separation between SiPMs to 25 mm and $\delta t \sim$ 400 ps

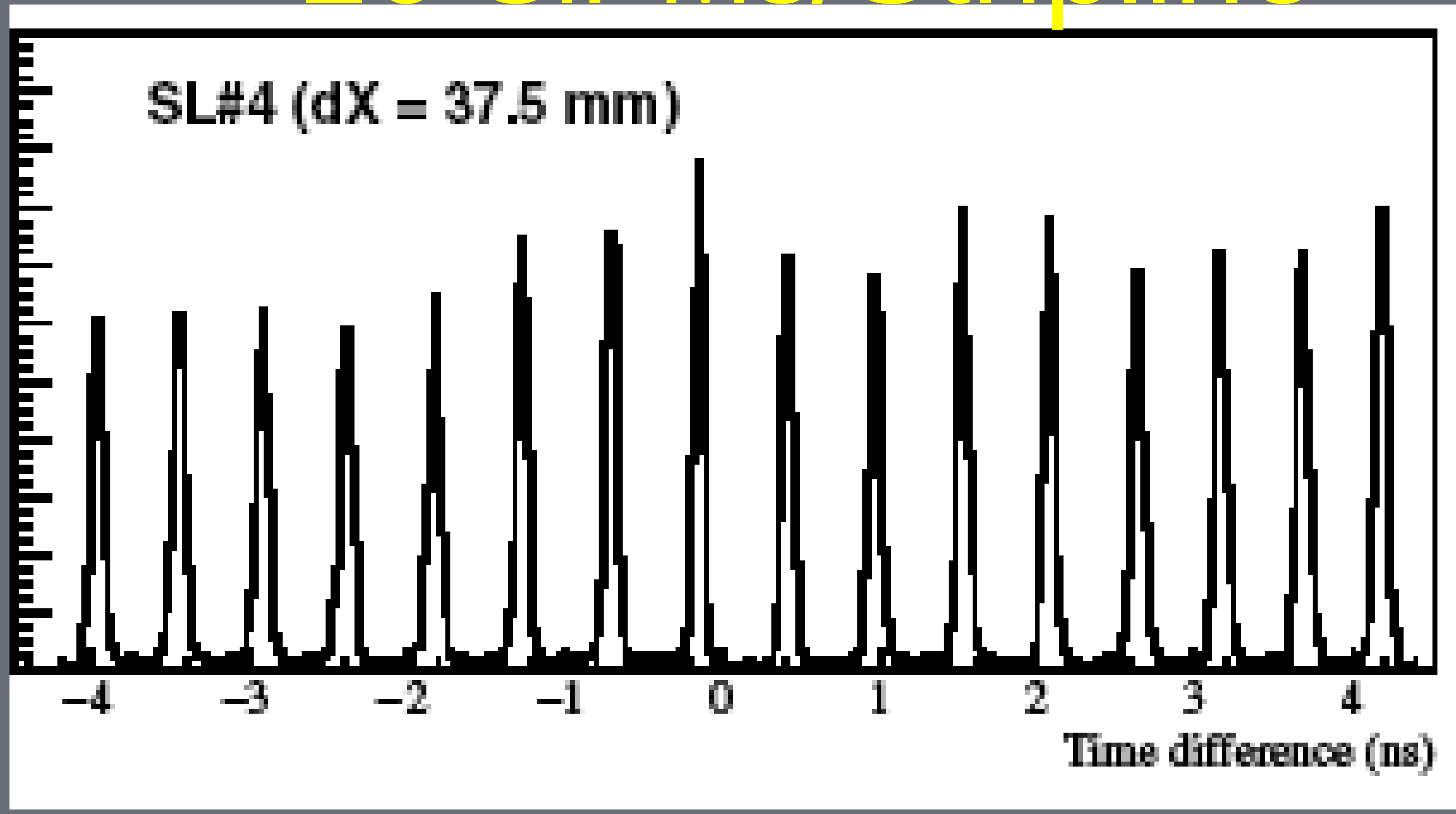


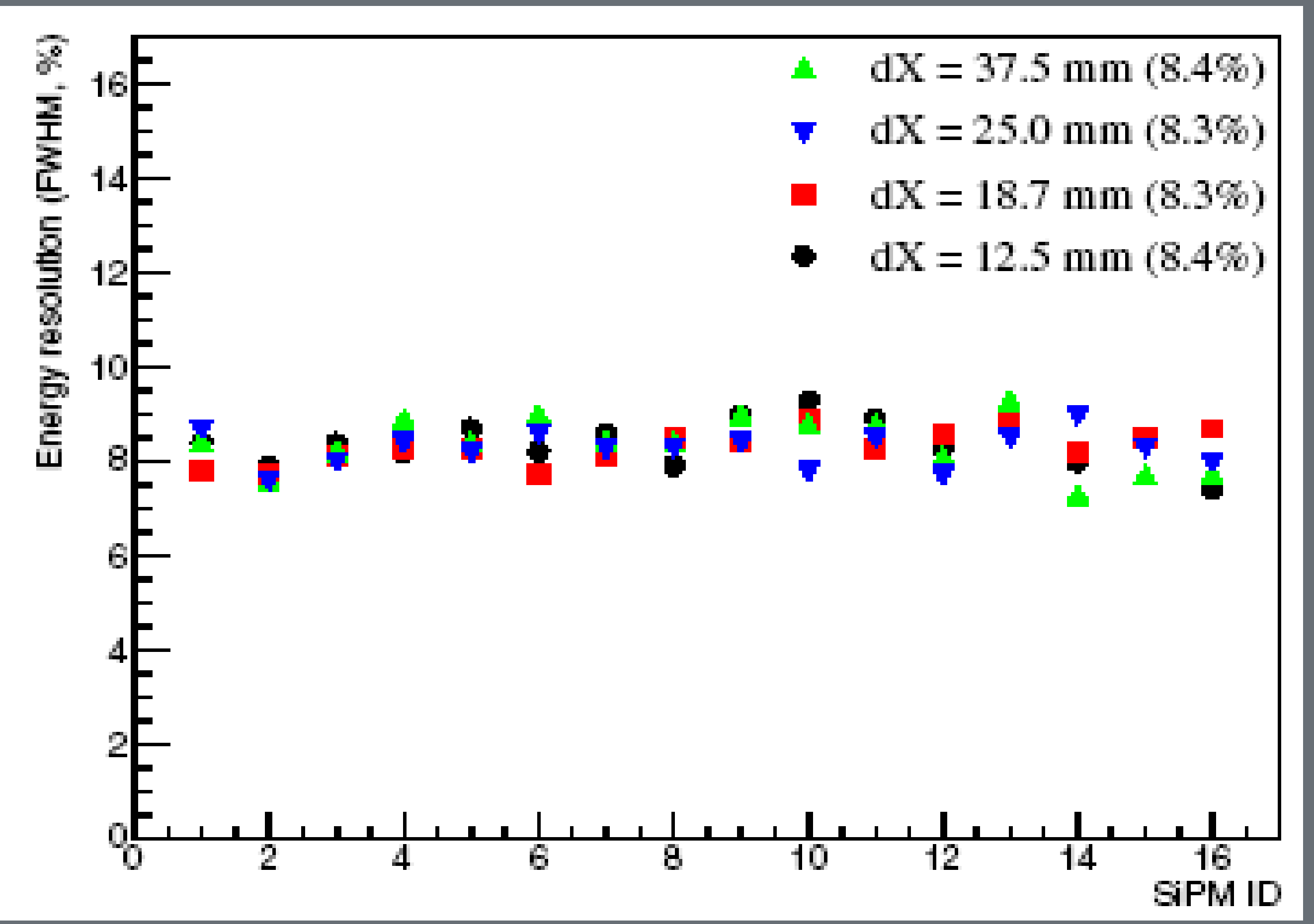


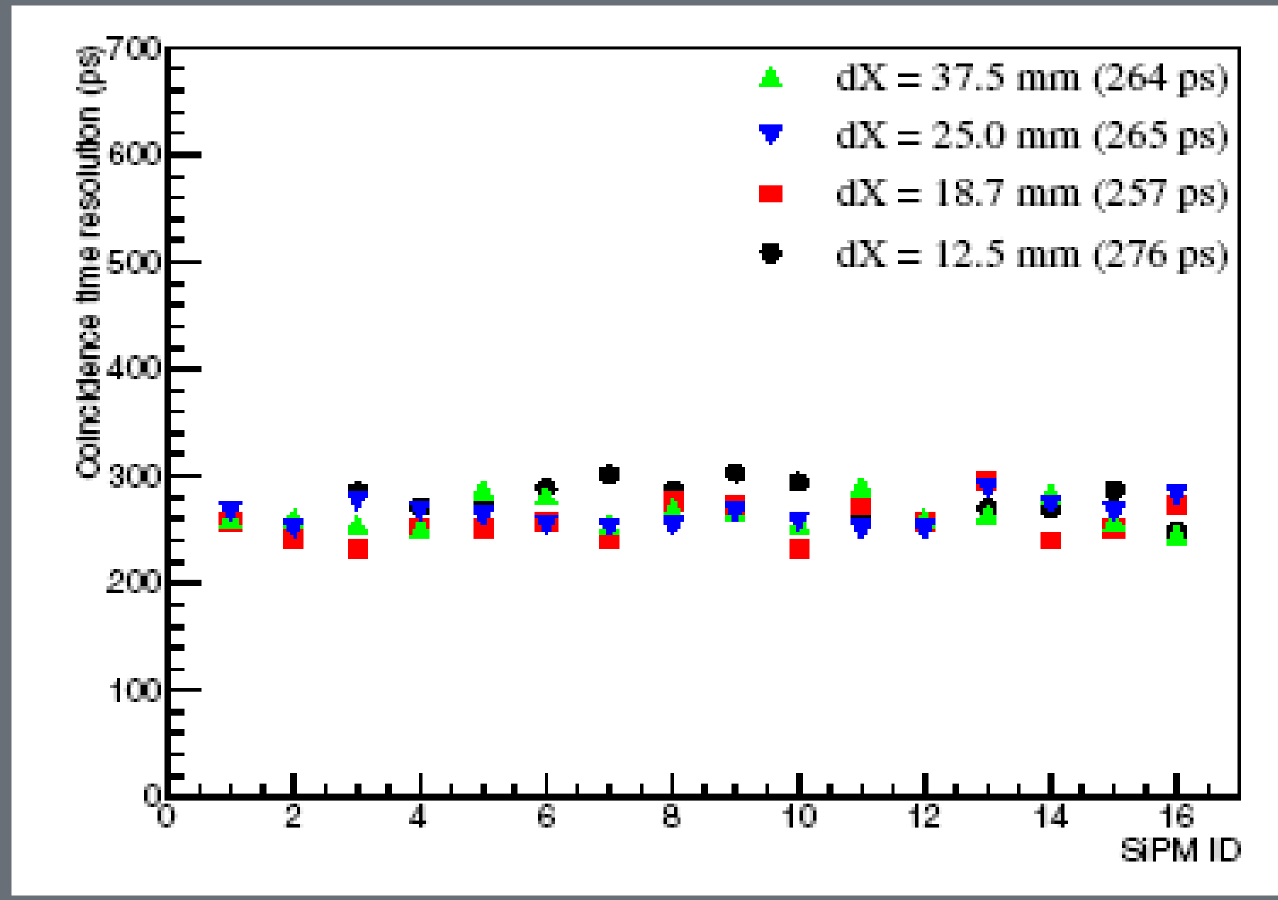


Stripline Readout is Scalable

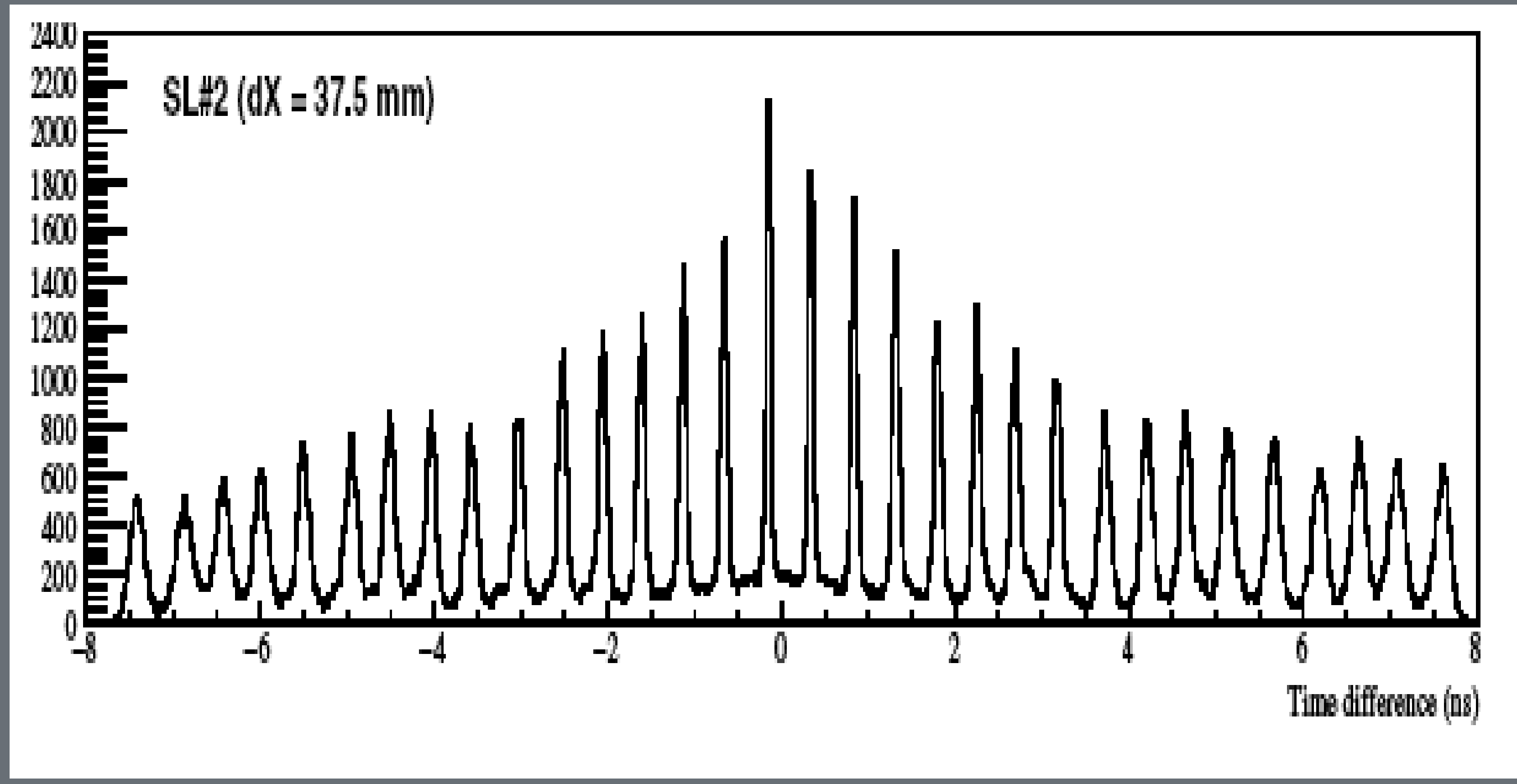
16 SiPMs/Stripline

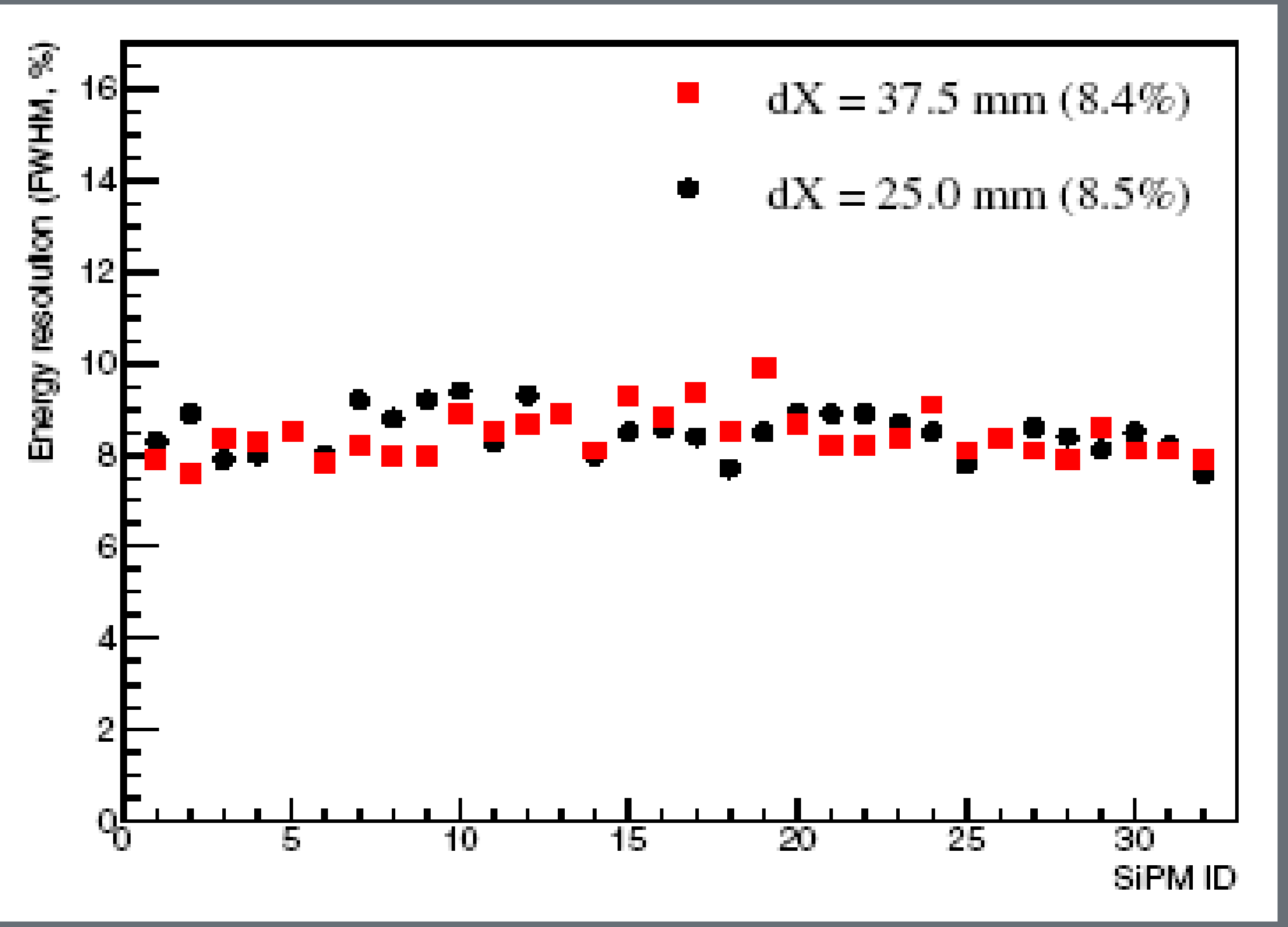


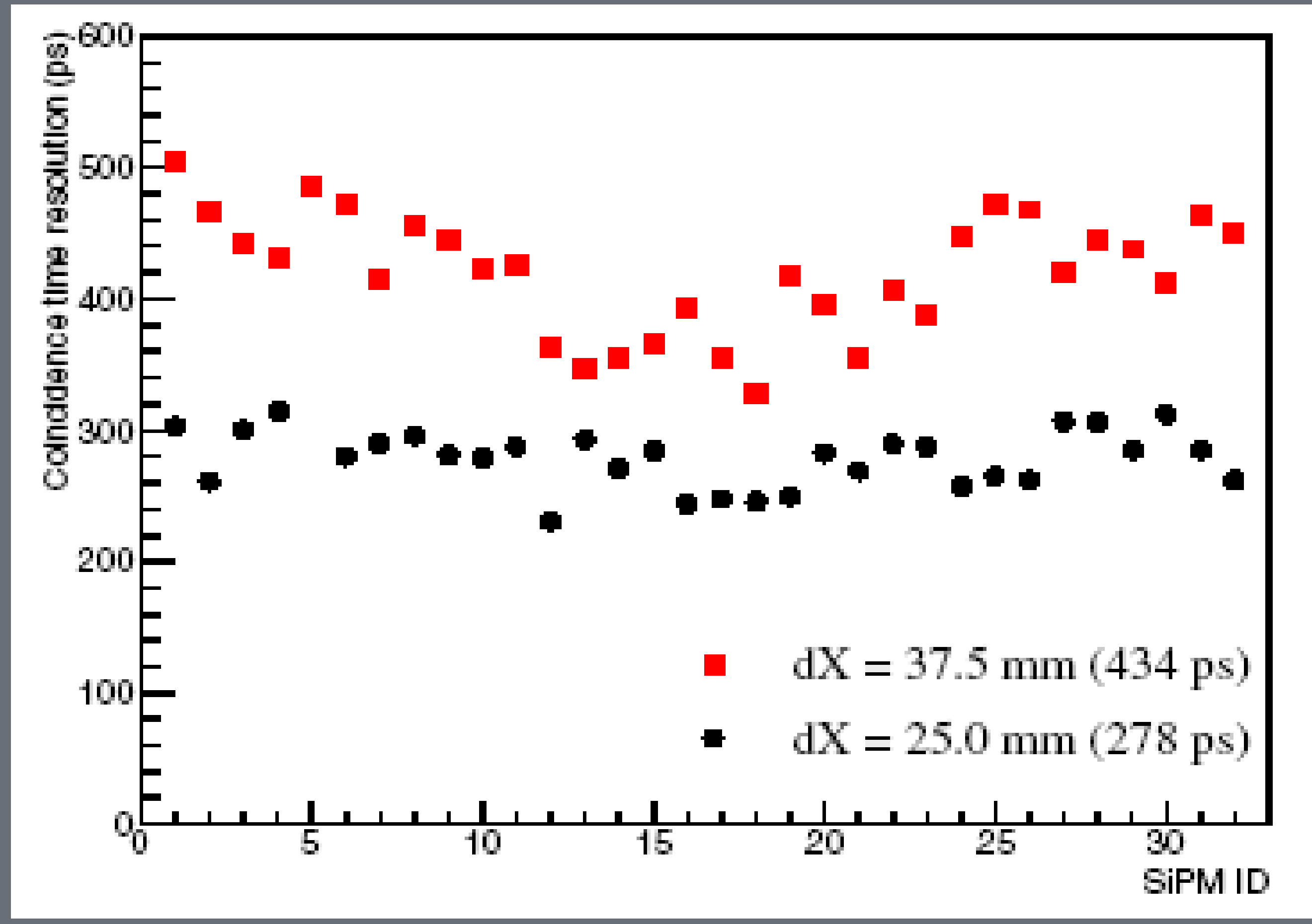




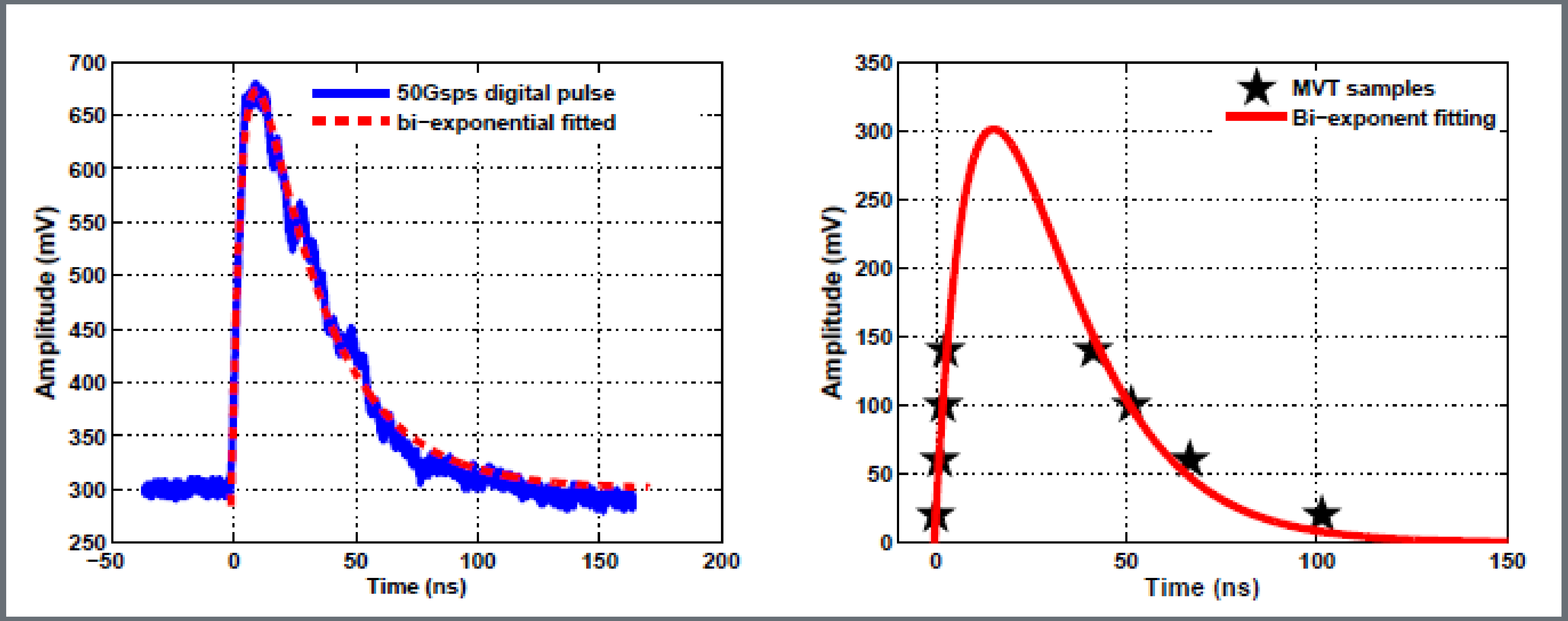
32 SiPMs/Stripline

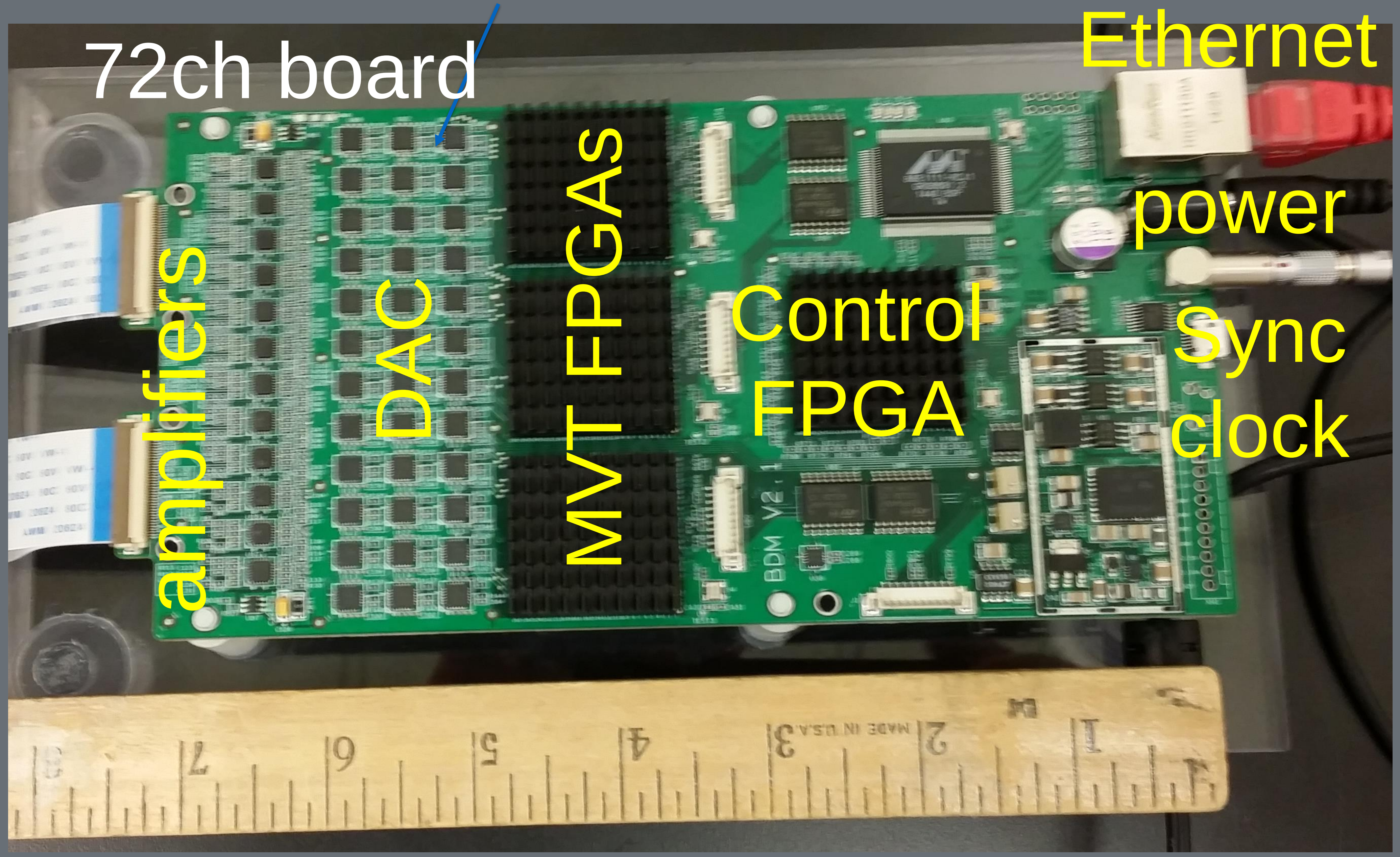






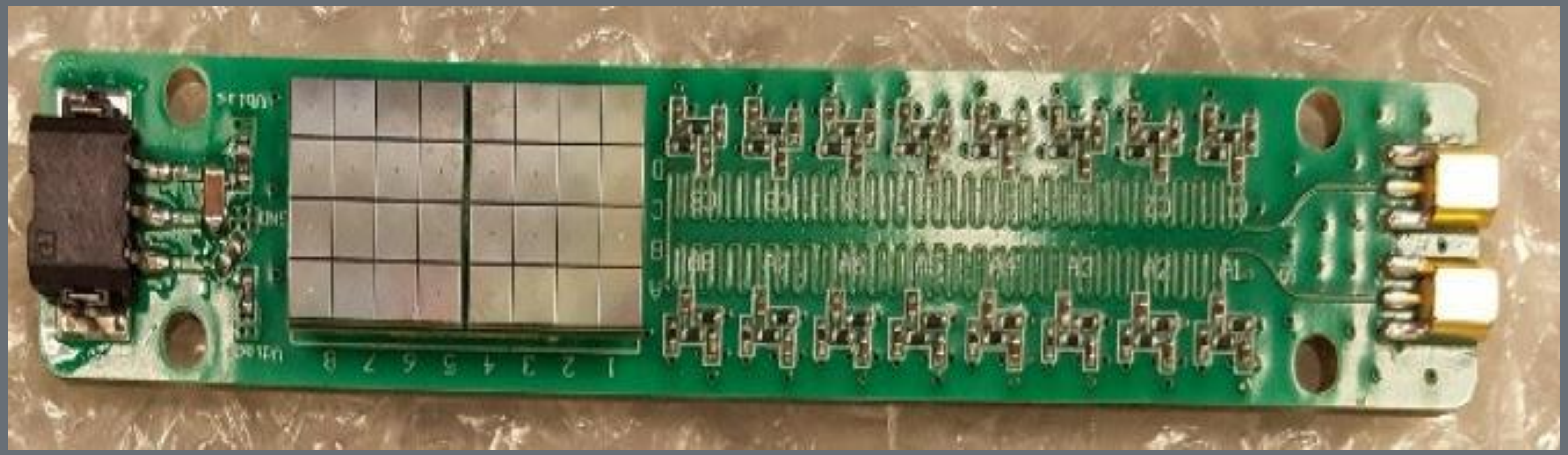
FPGA-only MVT sampling DAQ

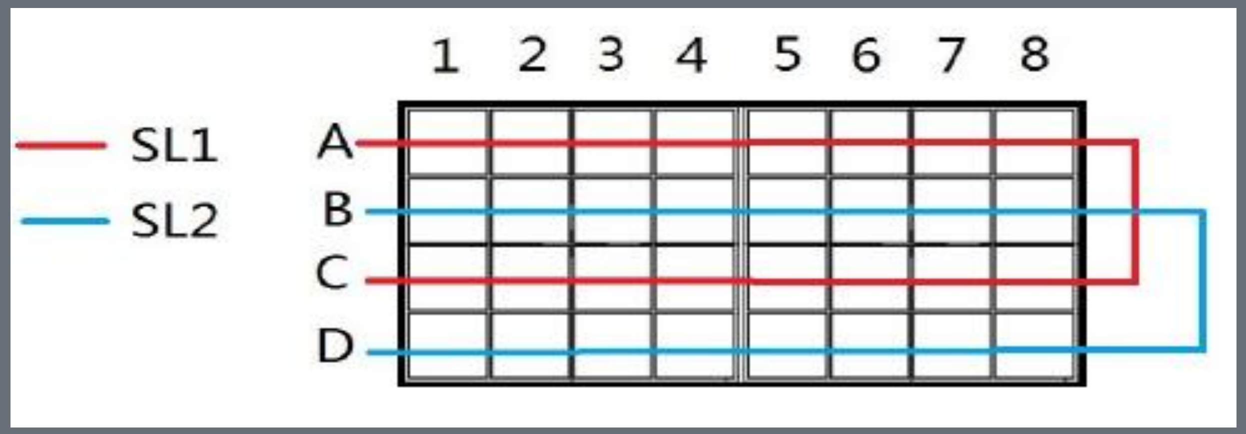




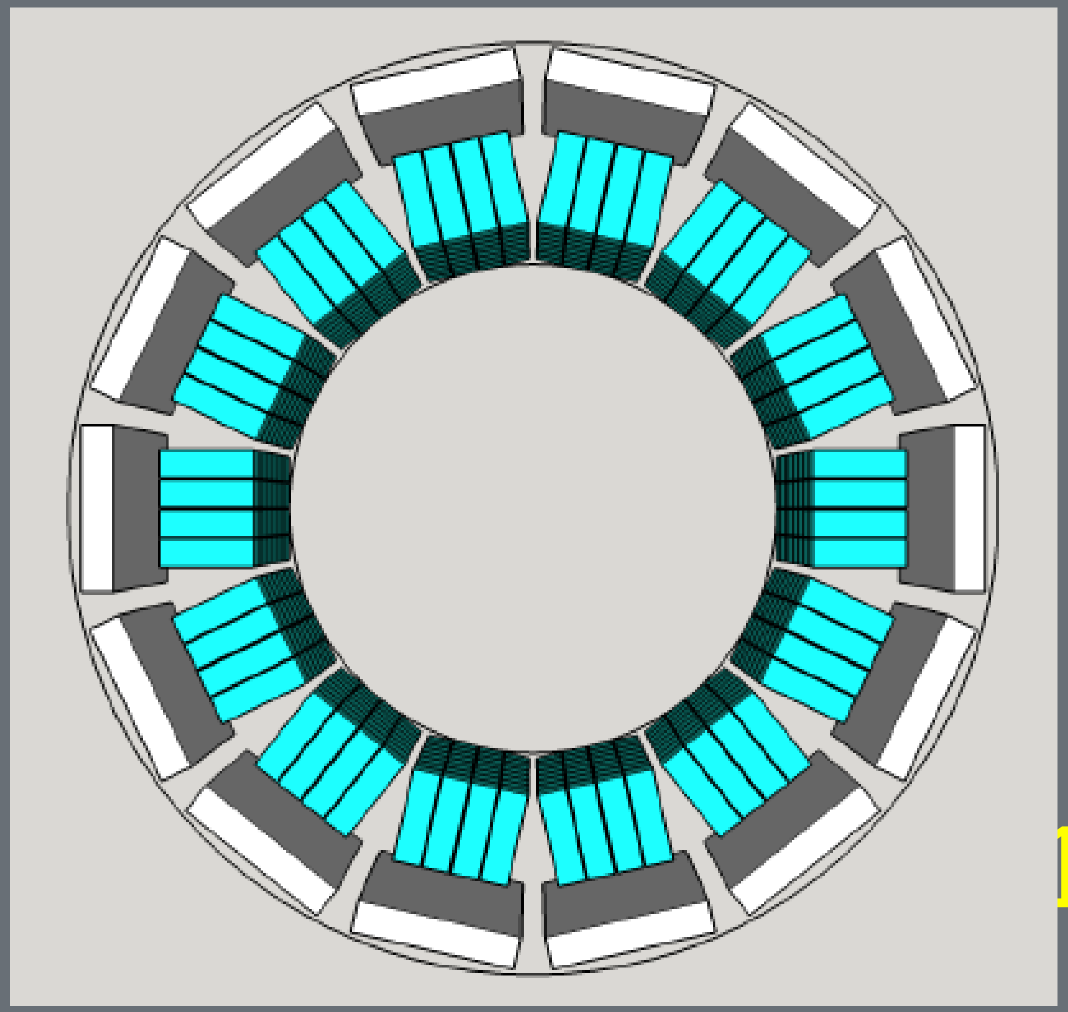
- Compact, high channel density
- FPGA based: affordable, flexible, upgradable
- Digital signal samples and serial digital output: robust, universal, digital signal processing
- Clean IO interface and network ready: rapid system development
- Do not require any proprietary parts and costly and length ASIC development
- Intrinsic time resolution ~ 300ps

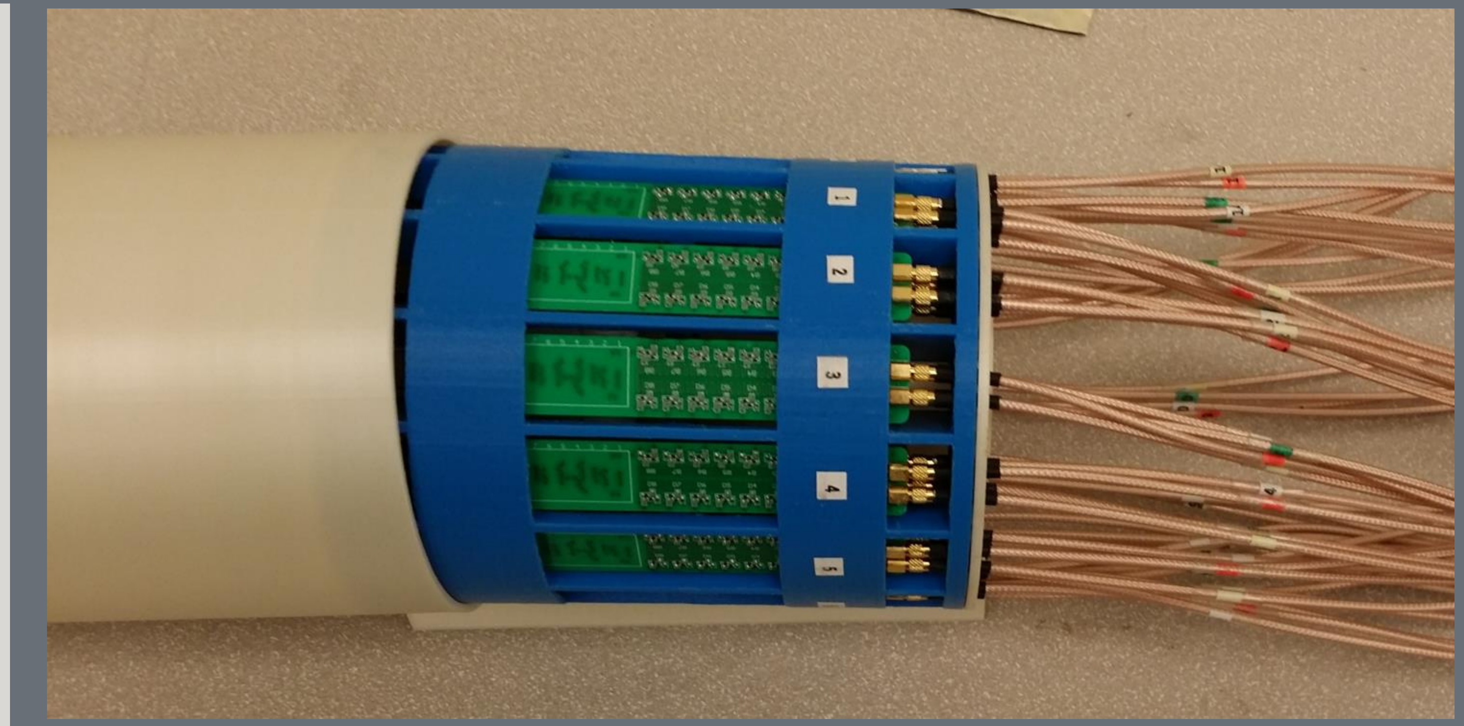
PET Insert



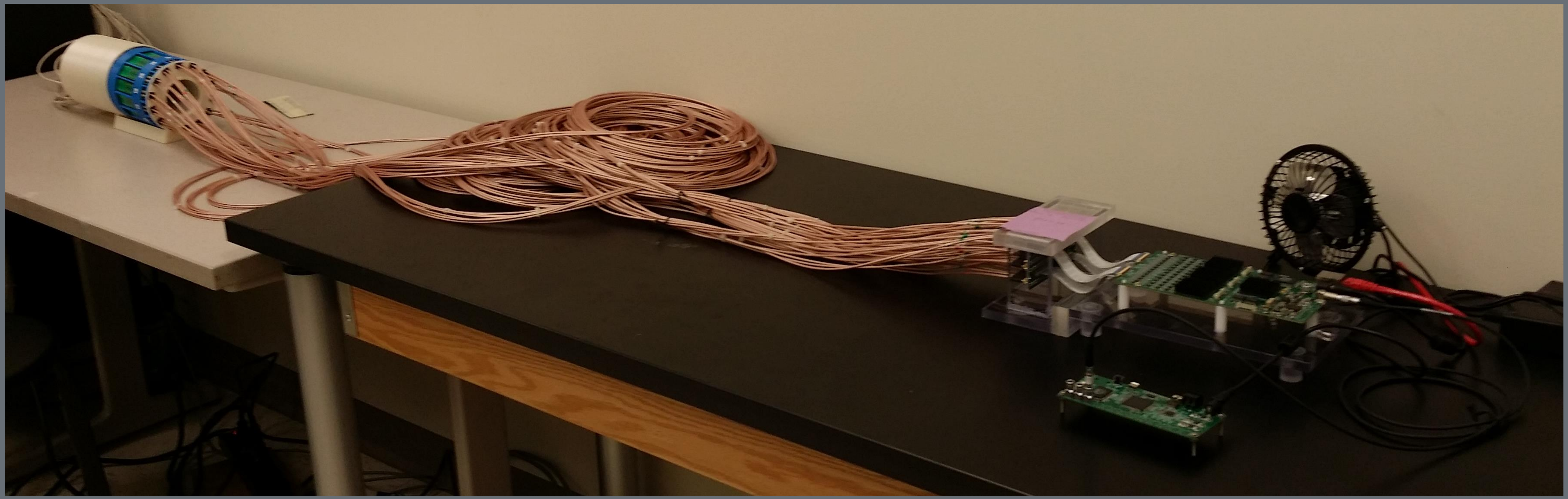


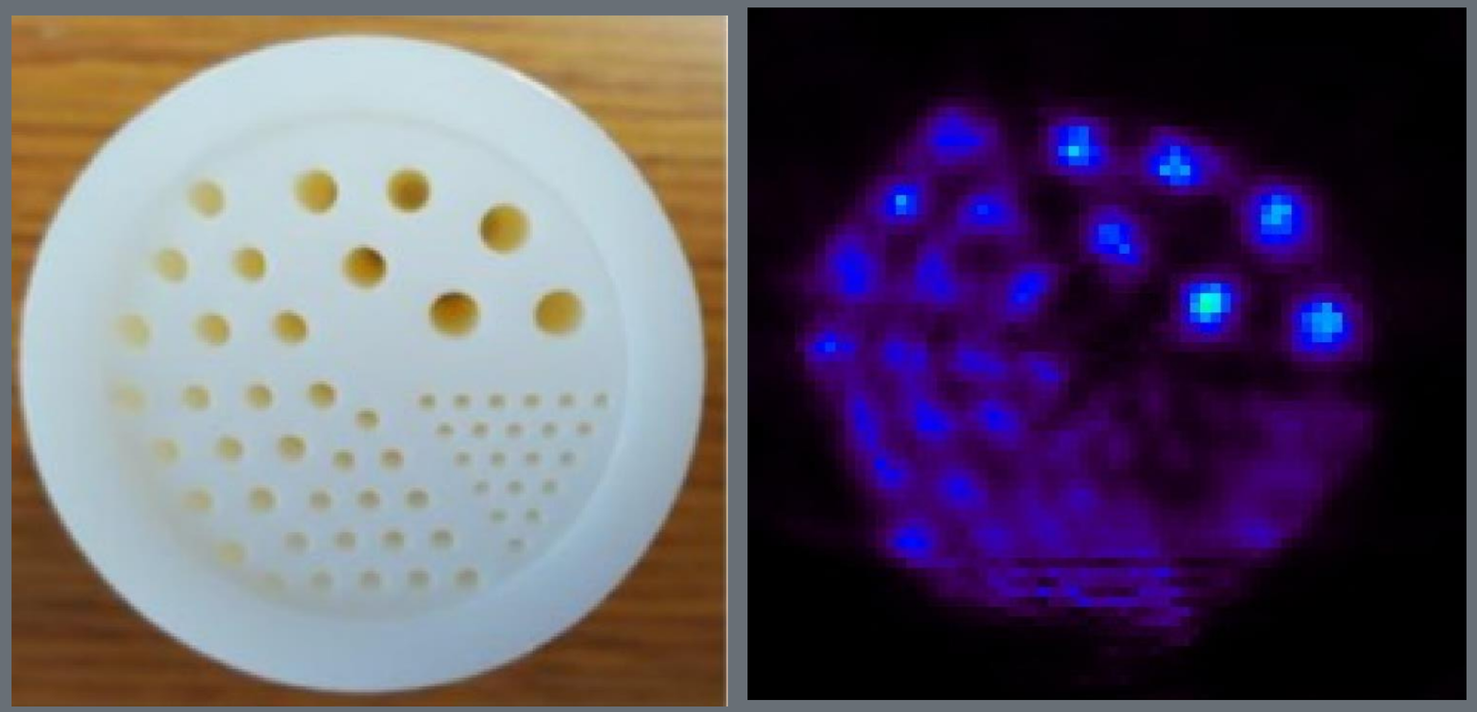
16 pxiels per stripline





14 modules; 2.5 cm axial FOV



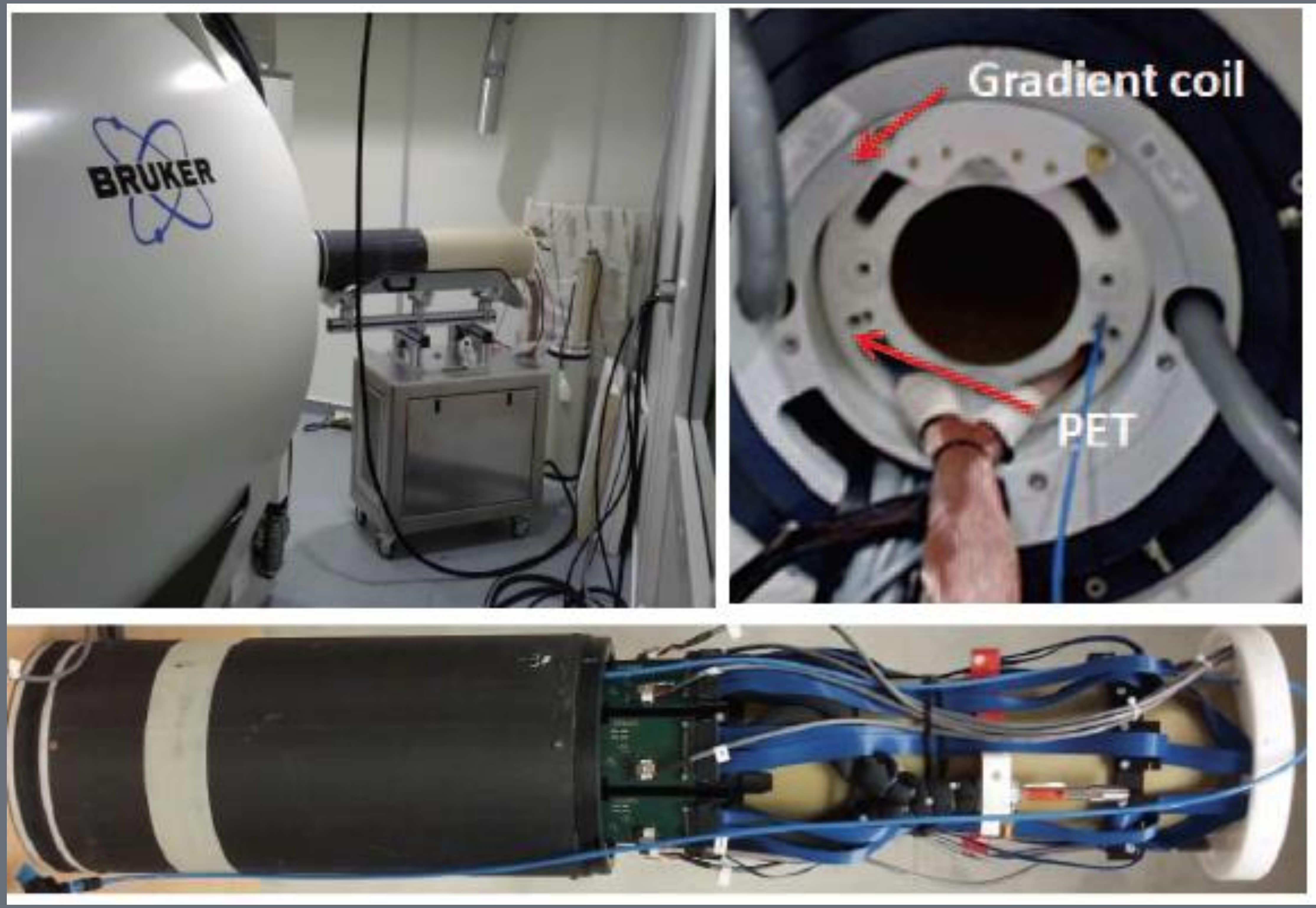


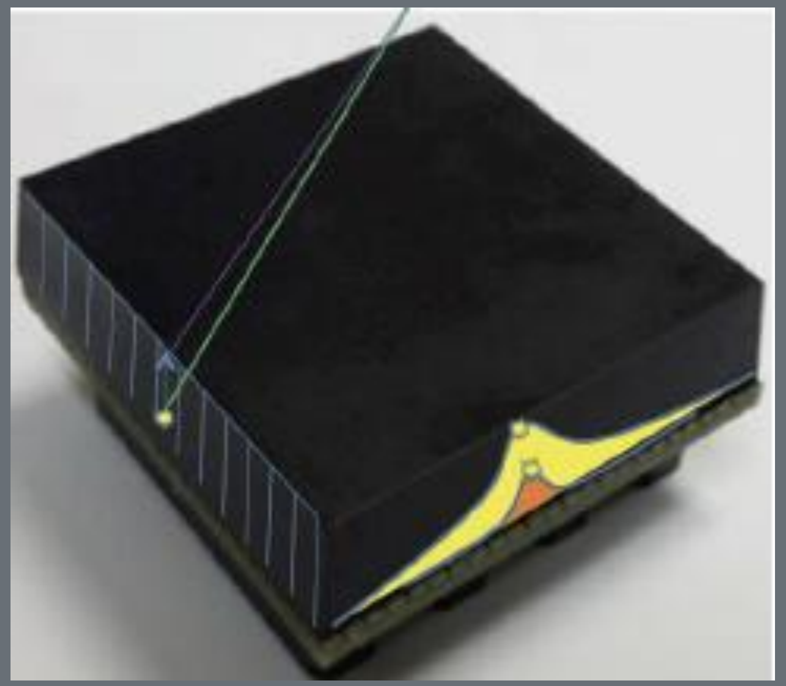
Initial phantom image
(3.0, 2.6, 2.2, 1.8, 1.4, 1.0 mm)

Stripline Readout/MVT DAQ

- **Substantial channel reduction**
  - Alleviating engineering issues: heat dissipation, power consumption, space constraint.
  - Cost saving
- Detached electronics
  - Compactness
  - mitigate RF and temperature control issues in PET/MR
- **Highly flexible, scalable DAQ electronics**
  - With SL readout, multiple detectors can be daisy chained
  - The DAQ provides high channel density and is affordable
  - The DAQ produces digital samples
  - Use commodity electronics components and industry I/O standards

Bruker Peclinical PET Insert

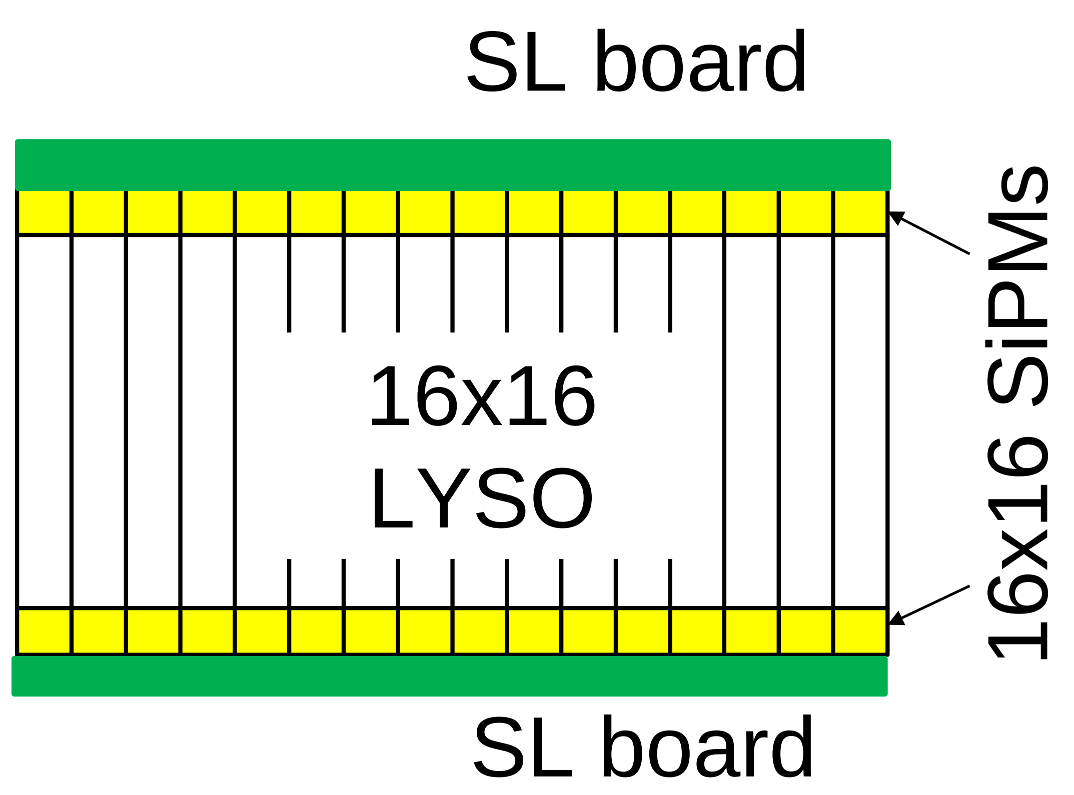


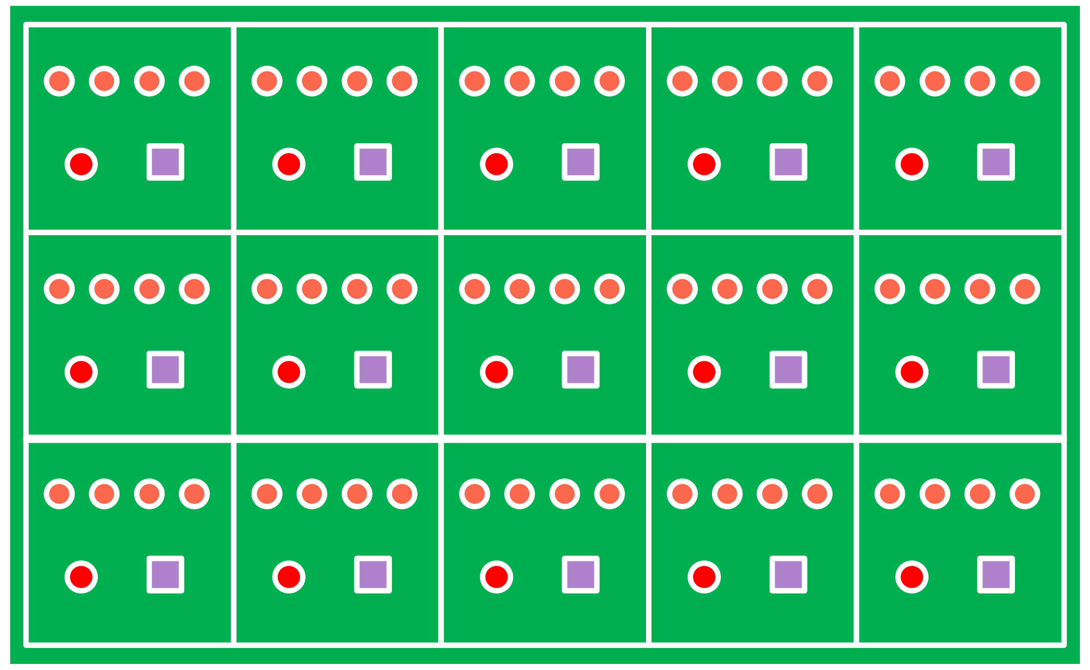


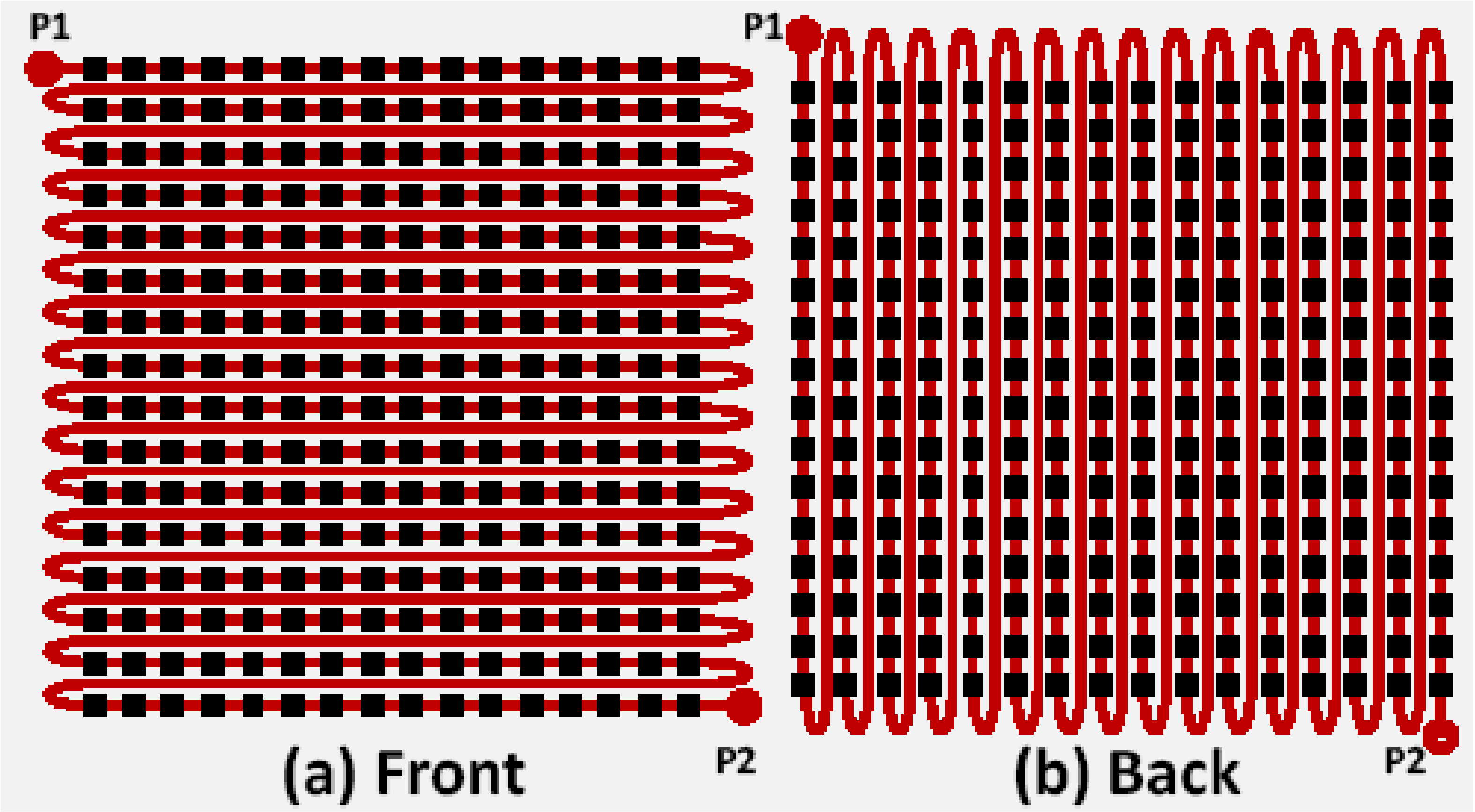
- eight 50x50x10mm continuous detector blocks, 12x12 SiPMs (SensL), resistive network row/column readout
- High resolution w/ DOI
- ID/OD = 114/198 mm
- Carbon Fiber RF shielding
- ~ 1m long

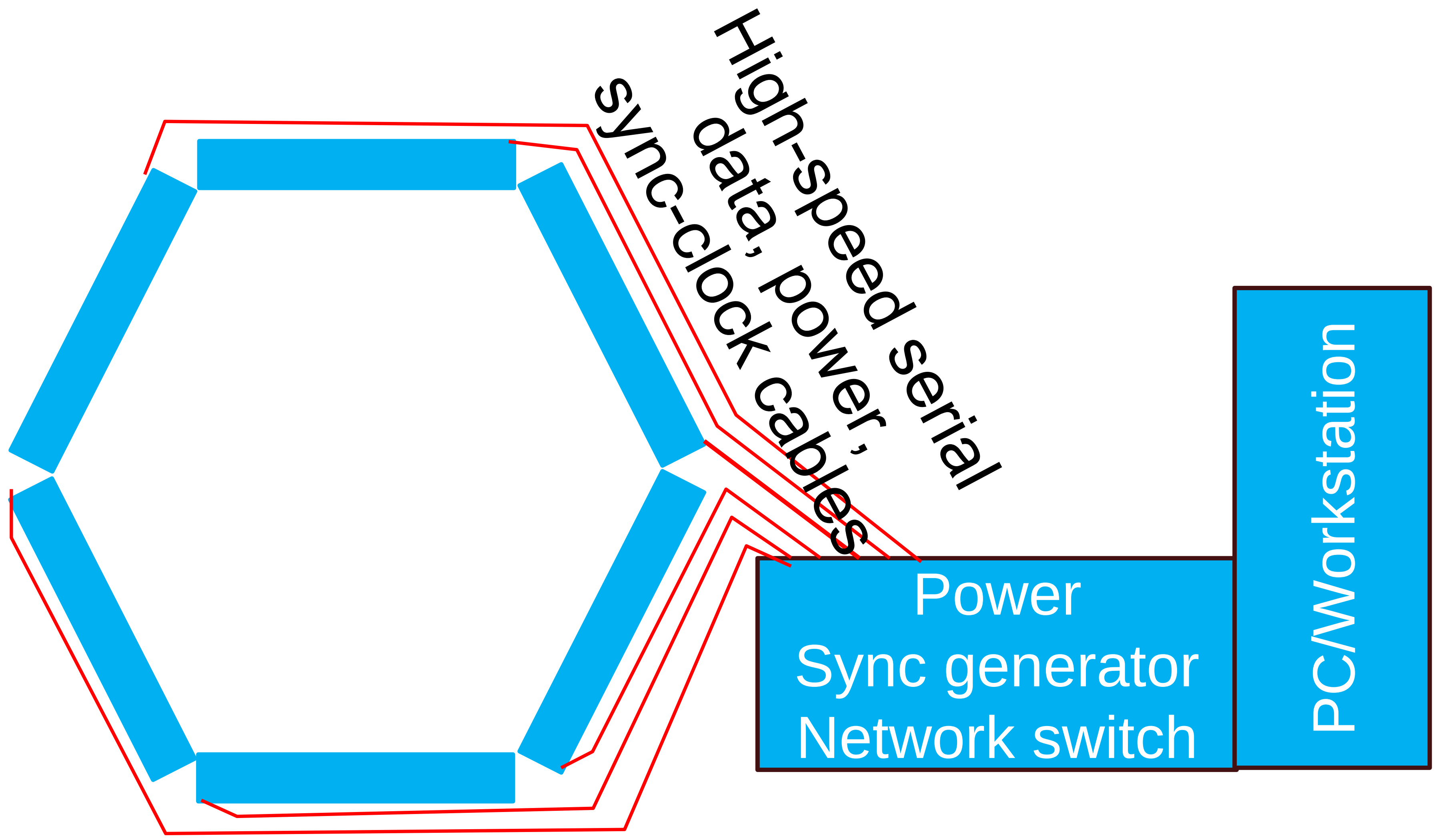
(AJ González, NSSMIC 2016)

Tilable Detector Block/Panel Detector









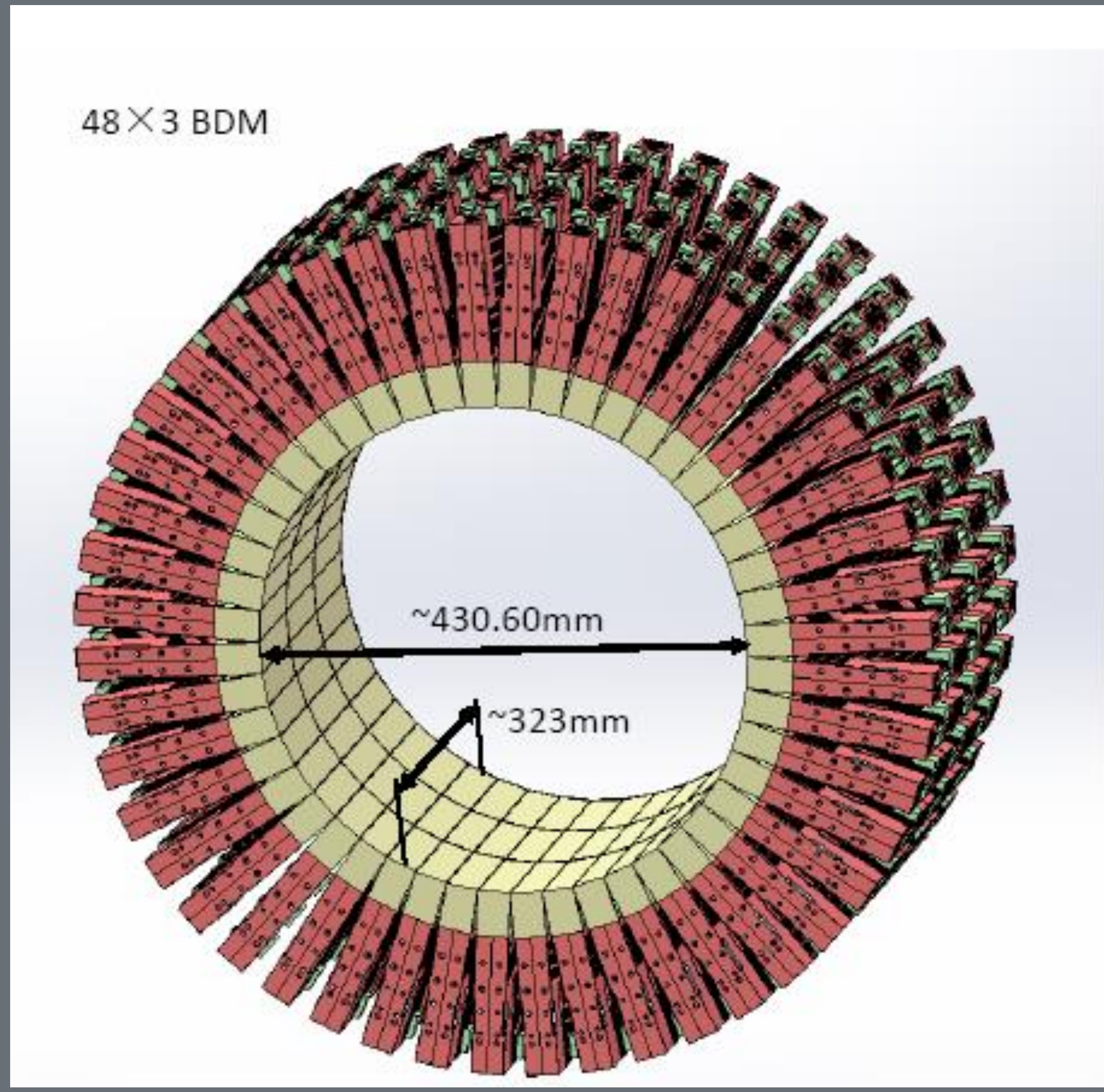
~50x50mm detector, 4 outputs per detector, DOI and TOF capable

Other trends: Dedicated Brain PET

- Need higher resolution (1-2 mm) and sensitivity for Brain imaging
- Mobile units can be useful for emergence care (stroke evaluation) and surgical room

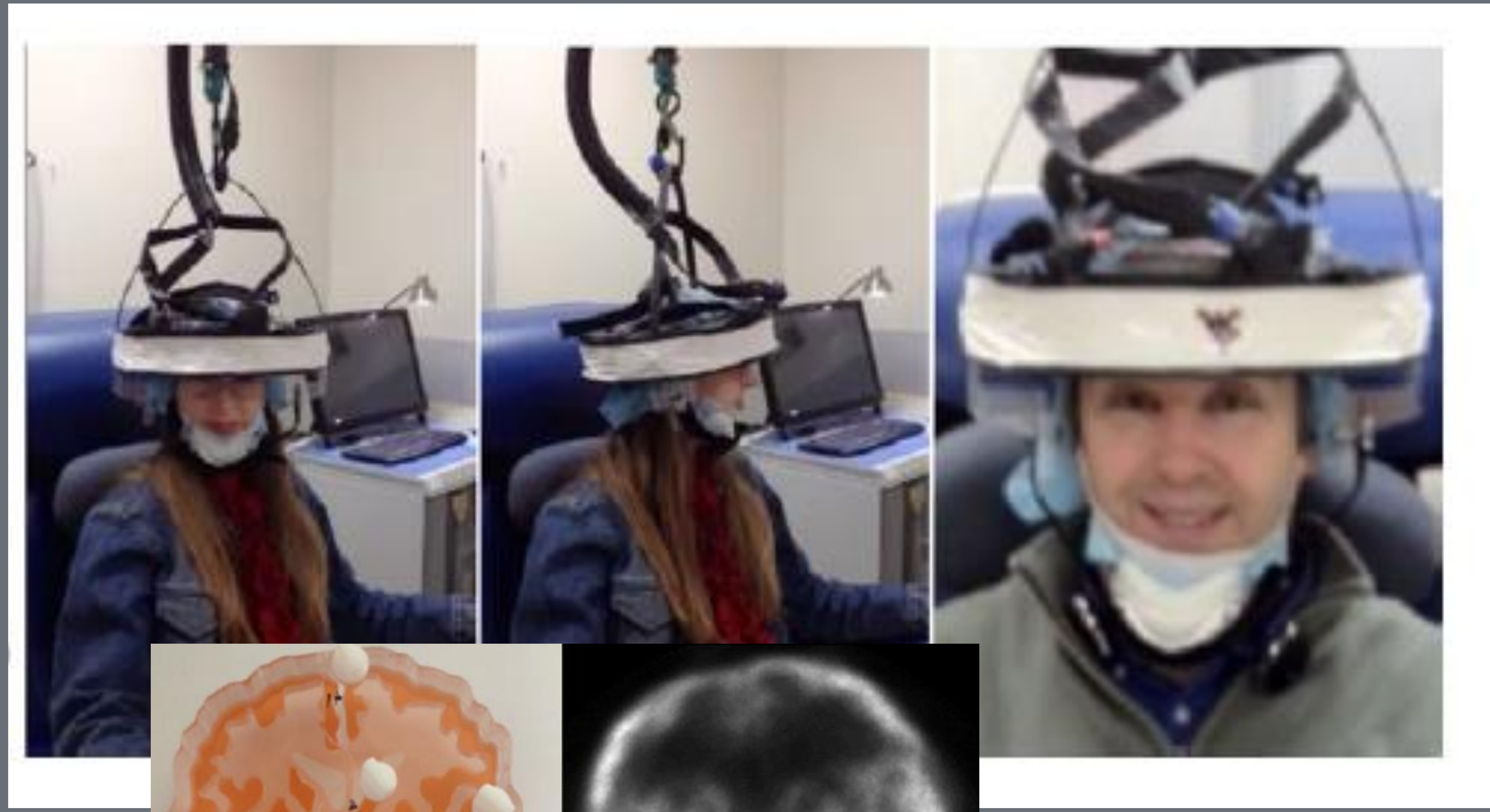
Siemens HRRT

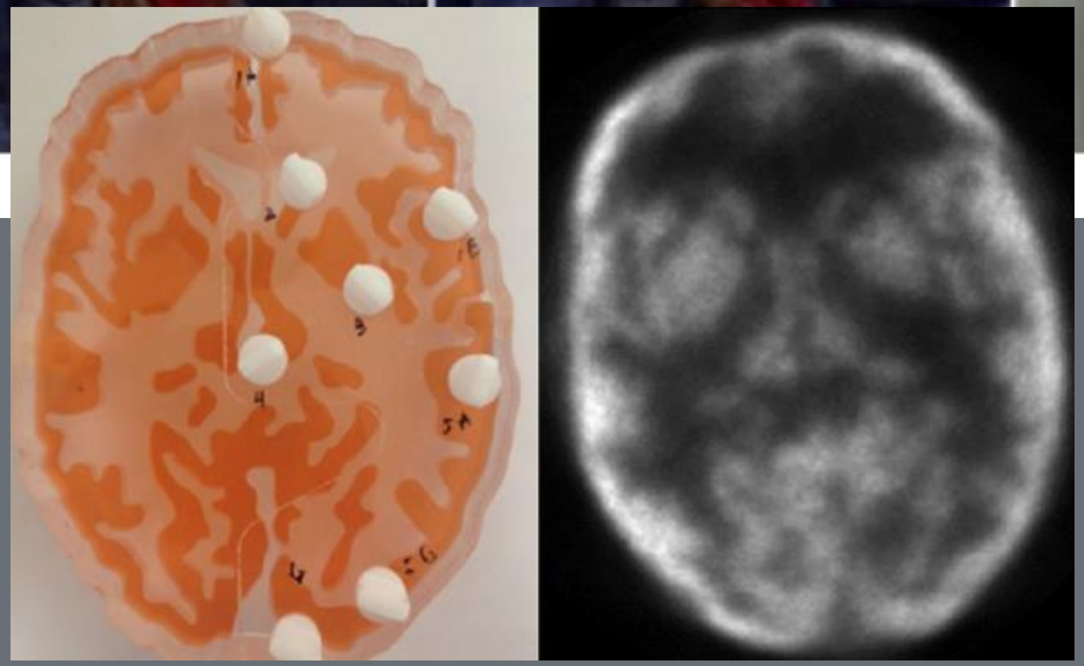
PhotoDiagnostic Systems (PDS) NeuroPET/CT



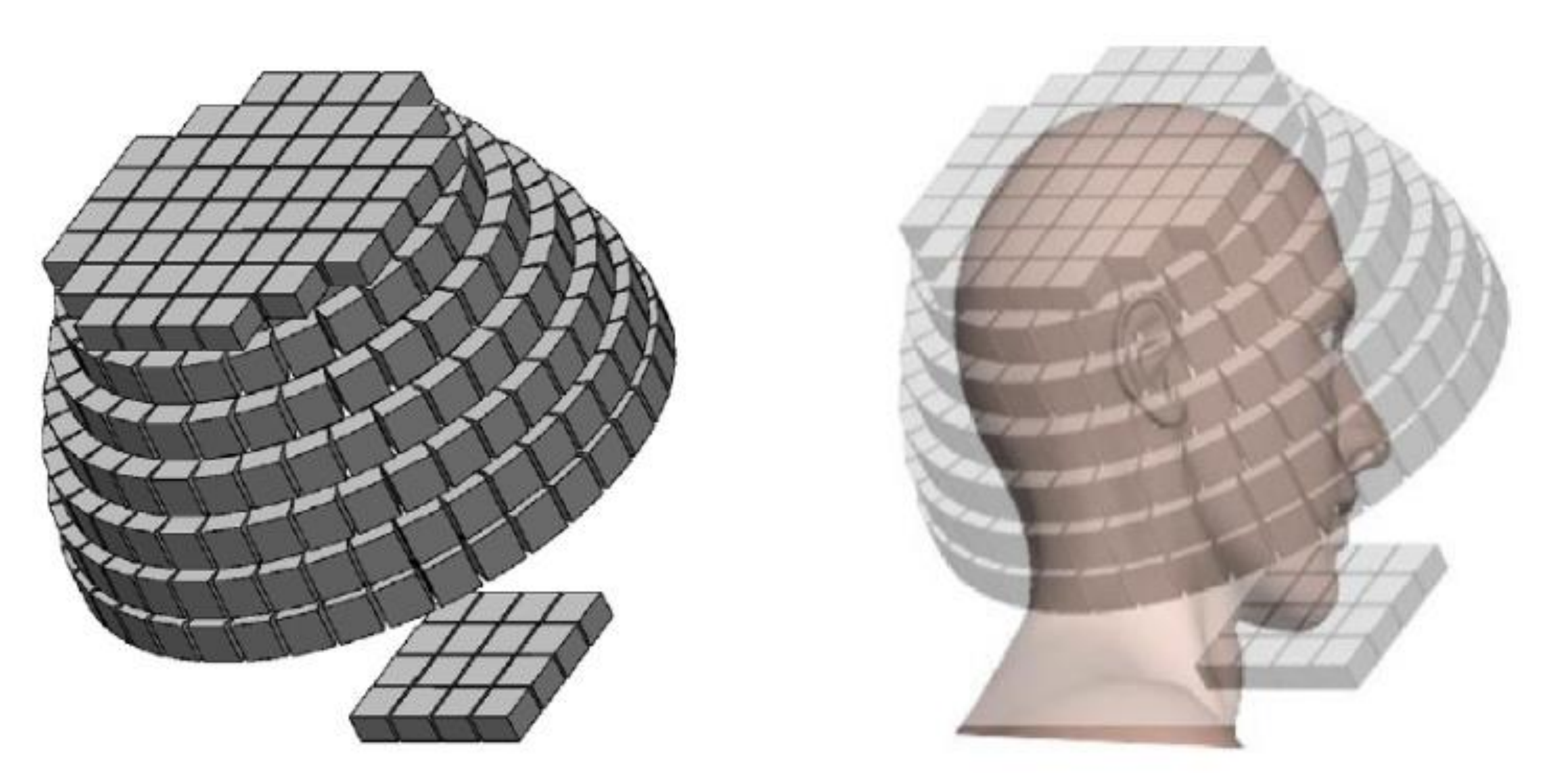
UChicago-HUST

Wearable Brain Imagers





(CE Bauer, Brain Behavior 2016)



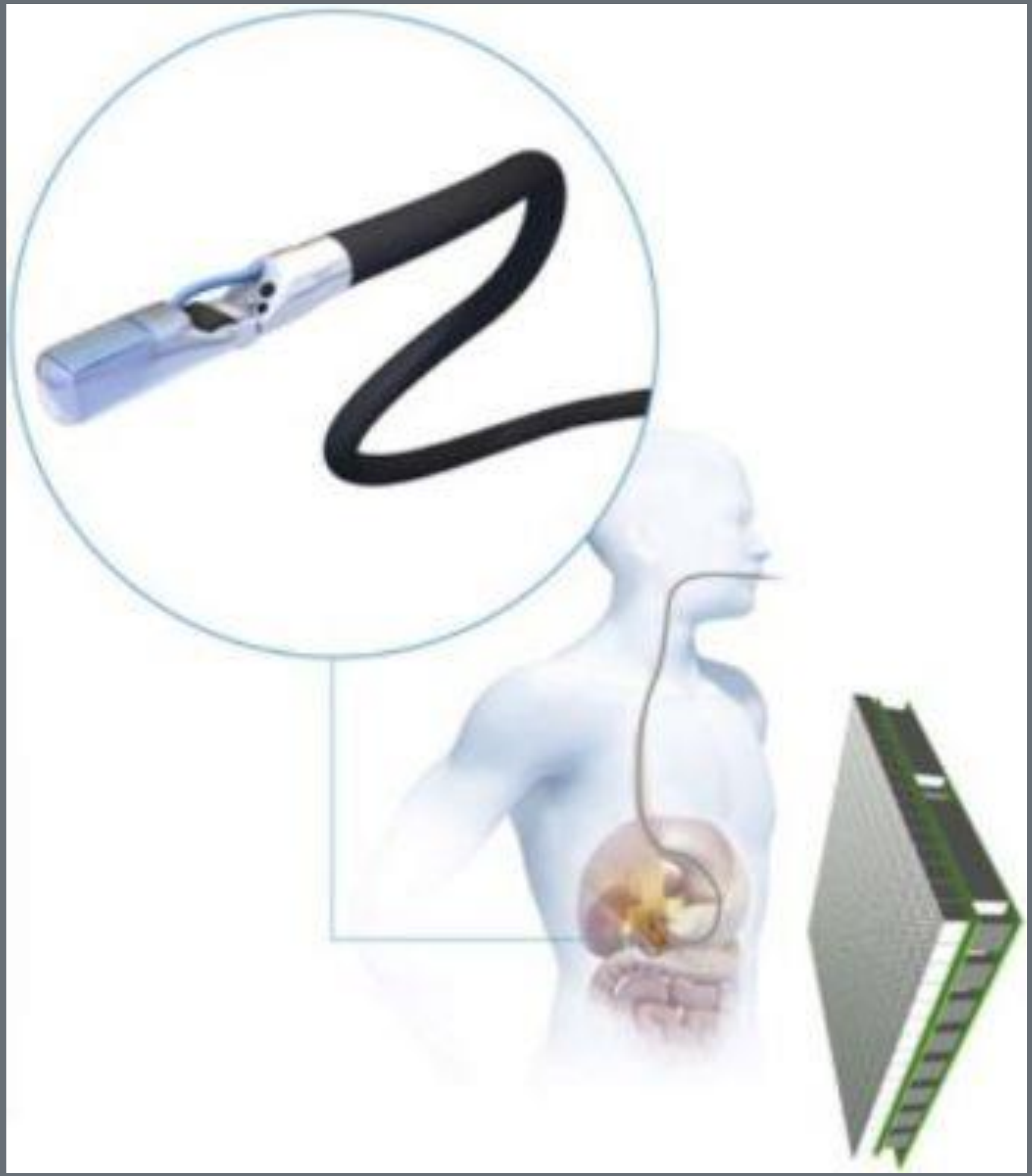
To optimize sensitivity and image quality

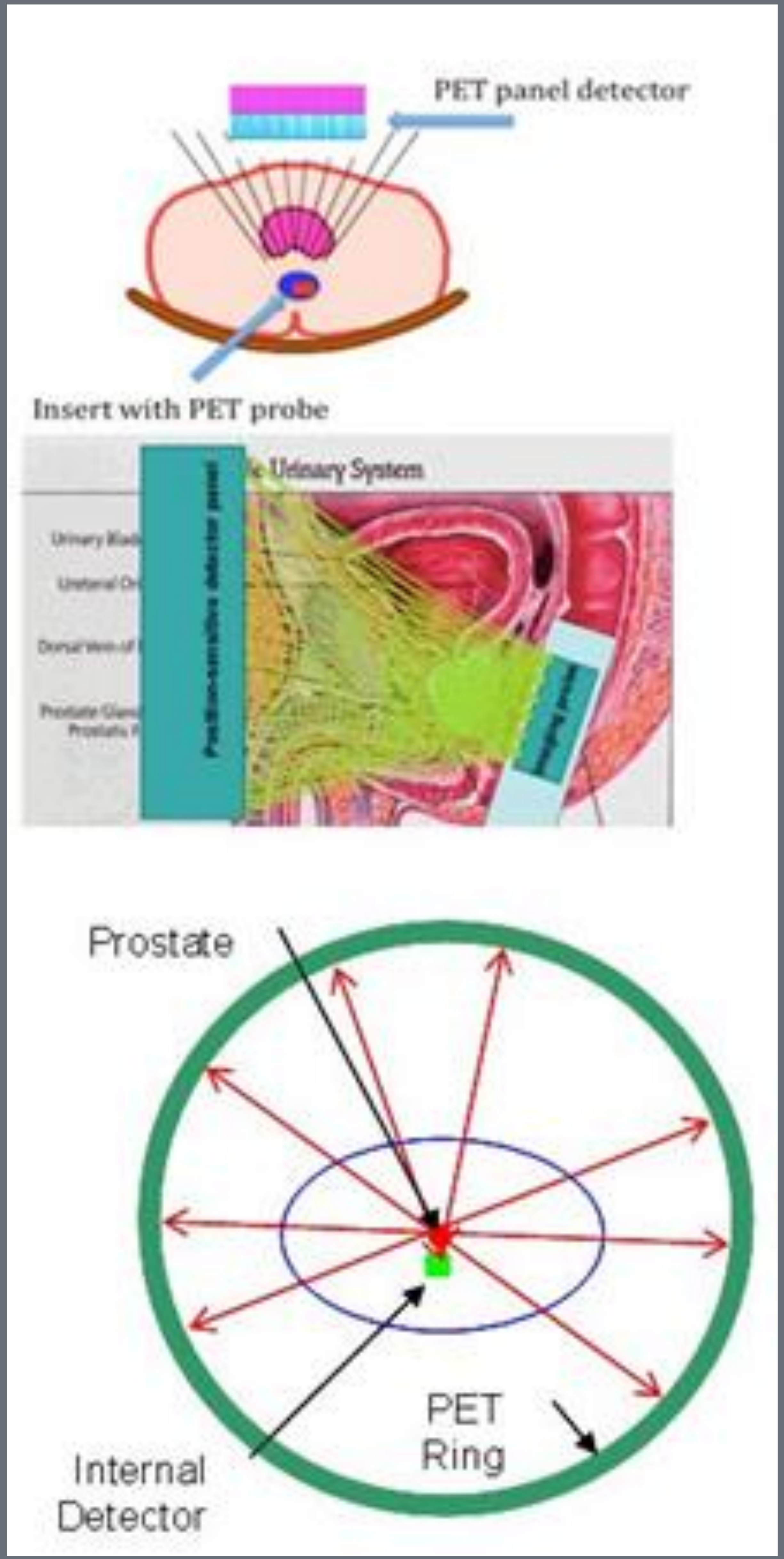
Other Organ-Specific Systems

PEM Naviscan

Newsoft Cardiac PET

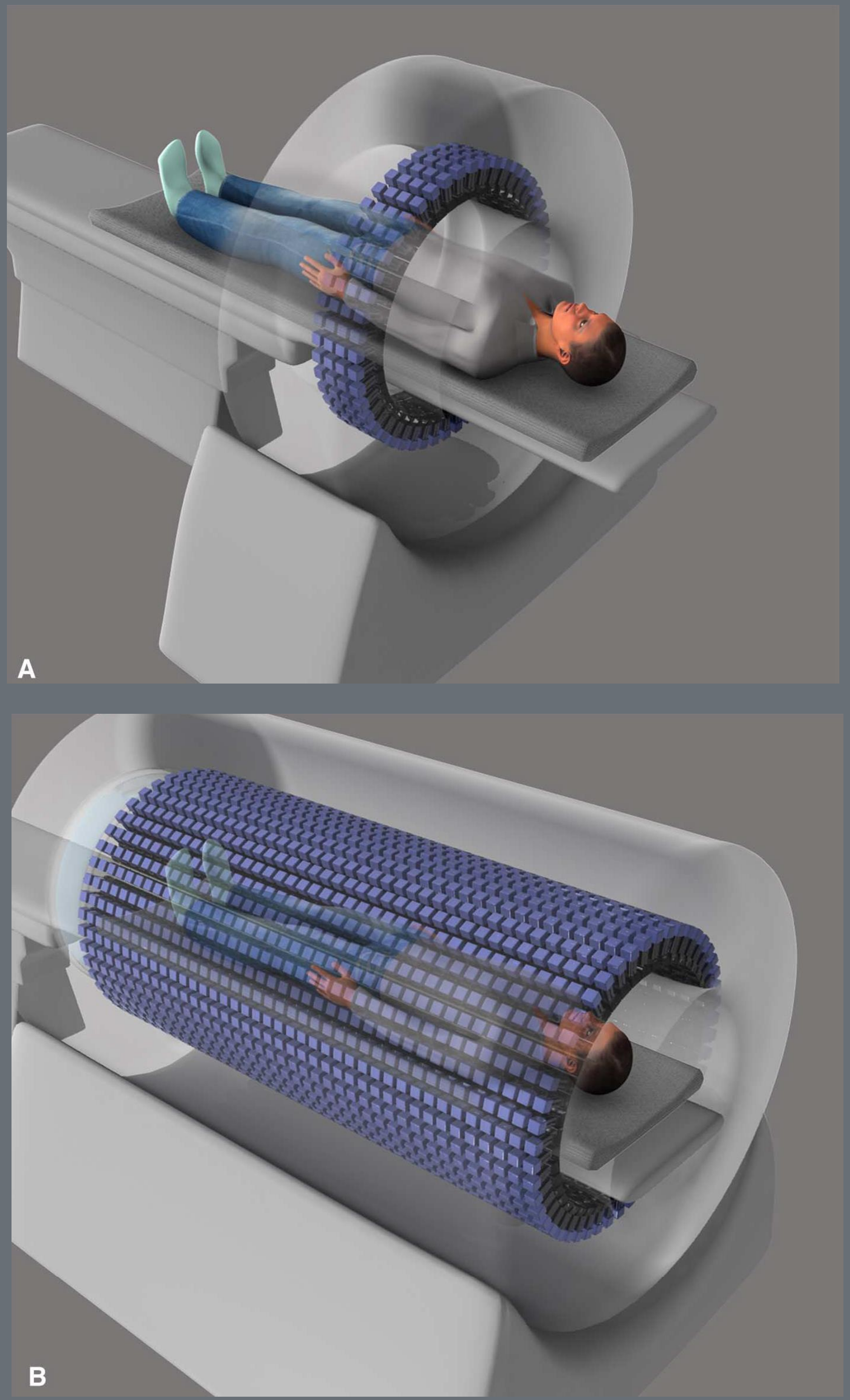
Probes





PET panel detector
Insert with PET probe
Prostate
PET
Ring
Internal
Detector

EXPLORER: Total Body PET



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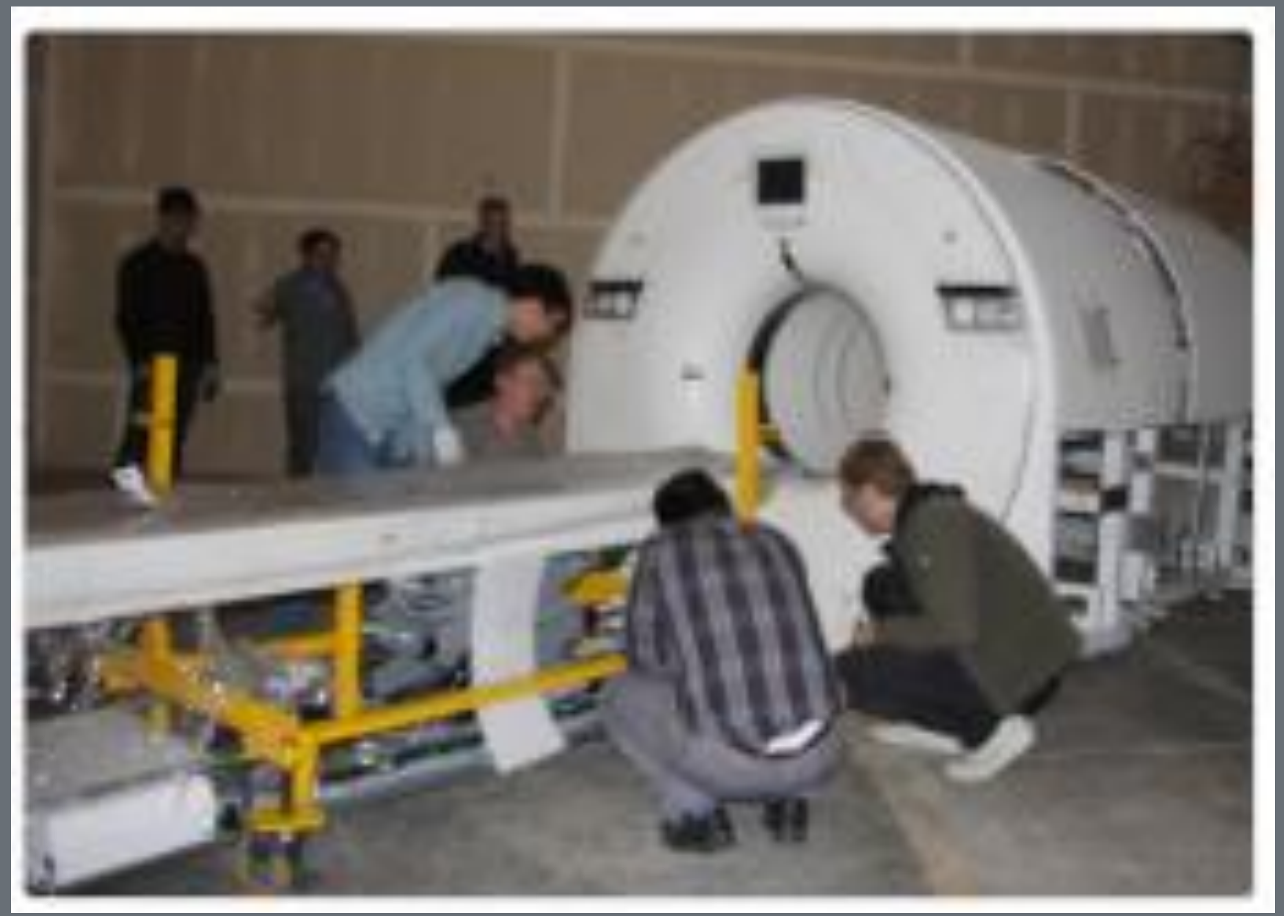
Berkeley Lab



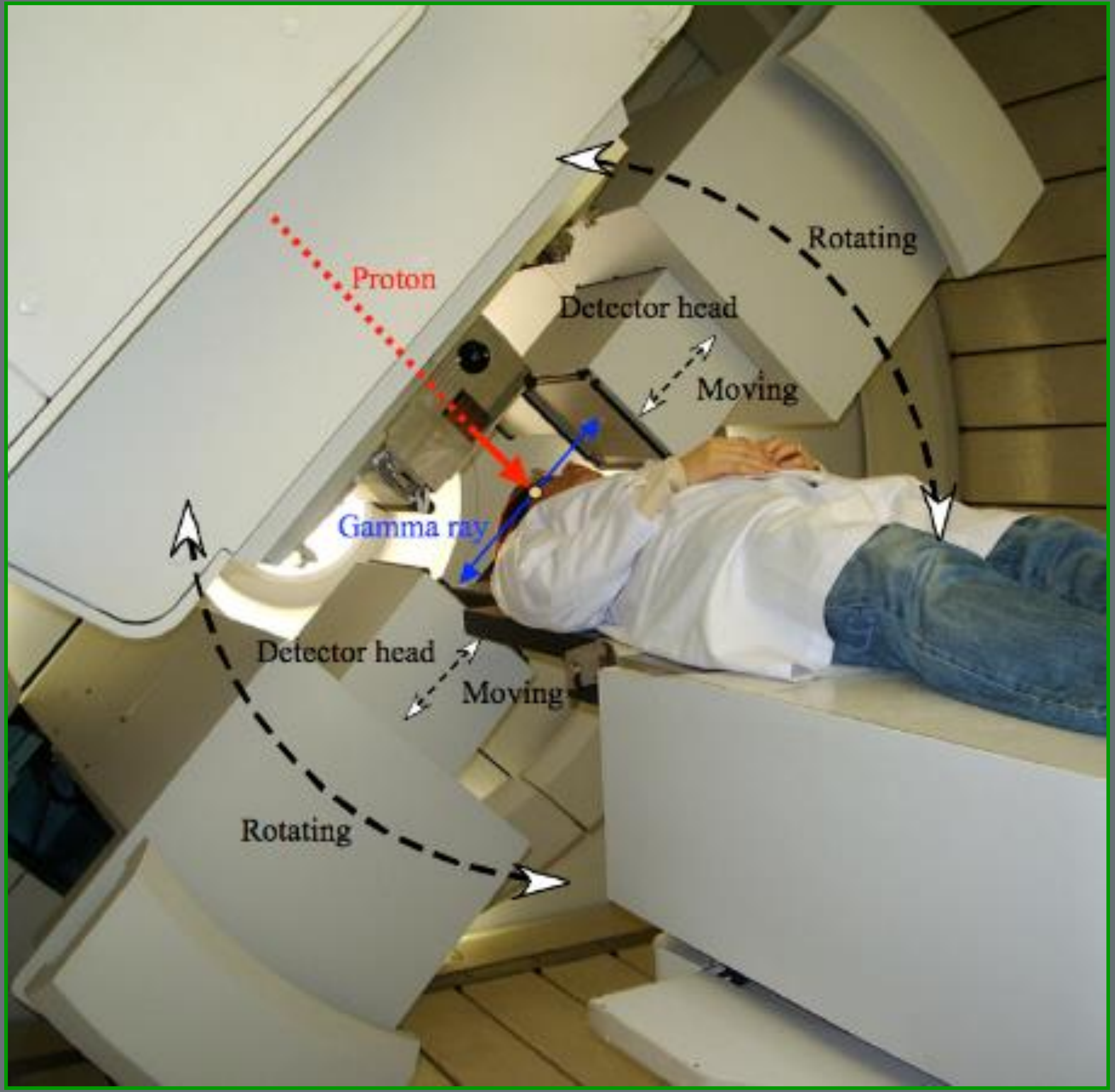
United Imaging

sensL
sense light

- **Systemic disease and therapies:**
  - Cancer: Ultra-staging and micrometastasis
  - Inflammation
  - Infection
  - Cellular therapy and trafficking
  - Mind-body interactions
- **Total body pharmacokinetics**
  - Drug development
  - Toxicology
  - Biomarker discovery
- **Low Dose may enable:**
  - Expanded use in pediatrics
  - Use in chronic disease
  - Studies of normal biology

From http://explorer.ucdavis.edu/

Proton therapy/In-Beam PET



T. Nishio et al.: Med. Phys. 33 (2006) 4190