FRCR Lecture IV

Nuclear Medicine



Positron Emission Tomography

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Remarkable people.
Extraordinary place.

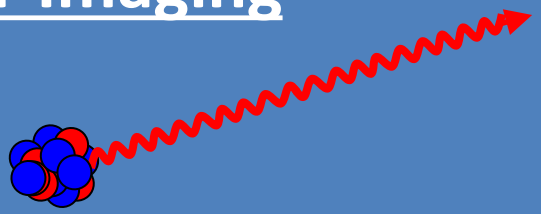
Image Acquisition Techniques

- Planar Imaging
  - Static
  - Dynamic
  - Gated
  - Whole Body / Continuous
- Tomographic Imaging
  - Single Photon Emission Tomography (SPECT)
  - Positron Emission Tomography (PET)

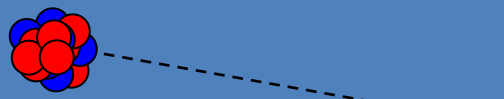
Functional Imaging – PET

What's the difference ?

SPECT Imaging



single gamma photon emission



positron emission

PET Imaging

Functional Imaging Isotopes

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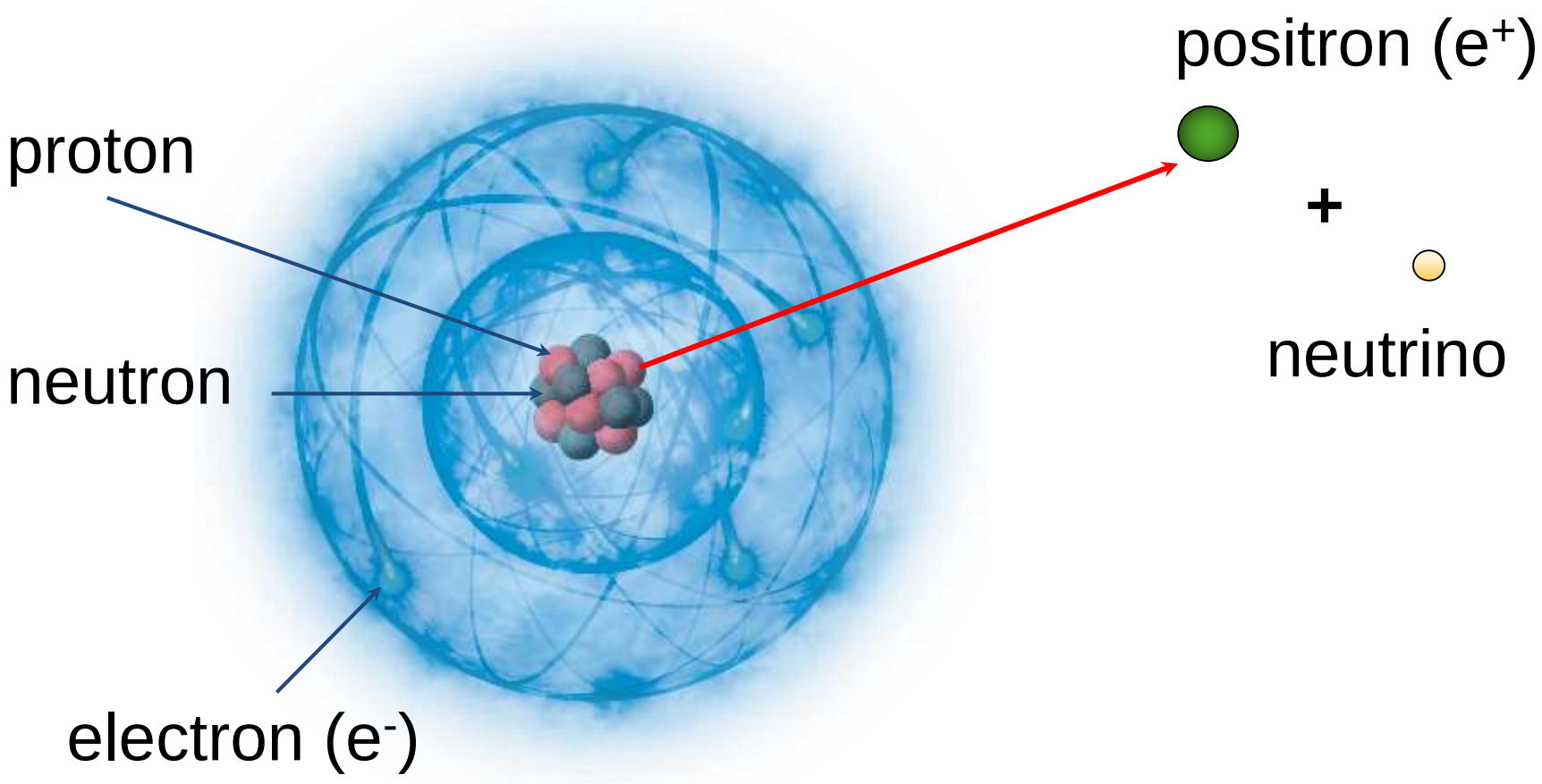
Planar/SPECT

Isotope	Half-life (hr)	Energy (keV)
^{99m}Tc	6.0	140
^{111}In	67.3	171 & 245
^{123}I	13.2	159
^{201}Tl	73.0	69-83

PET

Isotope	Half-life (min)	Energy (keV)
^{11}C	20.4	511
^{15}O	2.1	511
^{13}N	10.0	511
^{18}F	109.8	511

Radioactive Decay by Positron Emission



Annihilation Reaction



511 keV photon

$E = mc^2$

Annihilation reaction

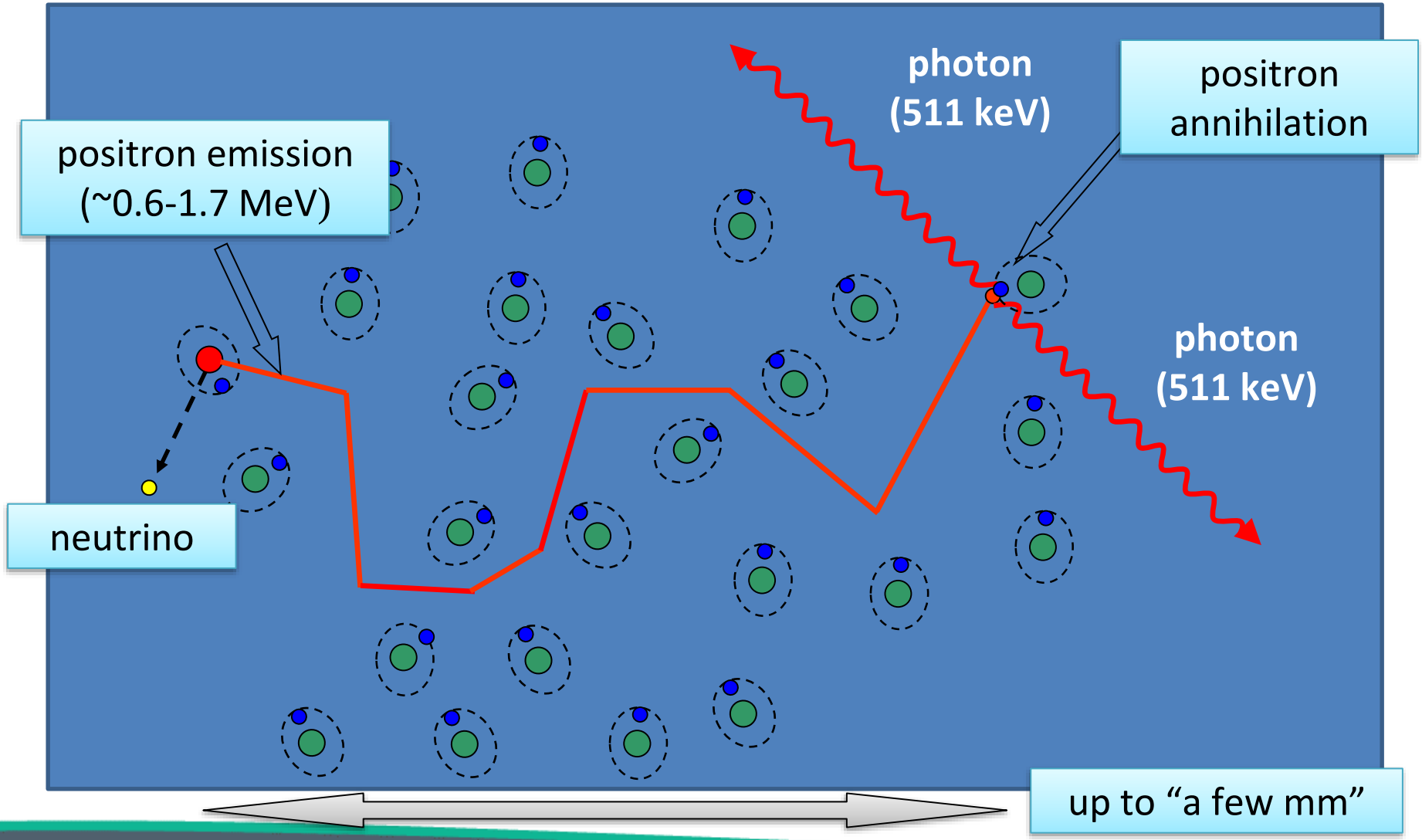
e+ + e-

Electron from material in body

Positron

511 keV photon

PET Isotopes



Properties of PET Isotopes

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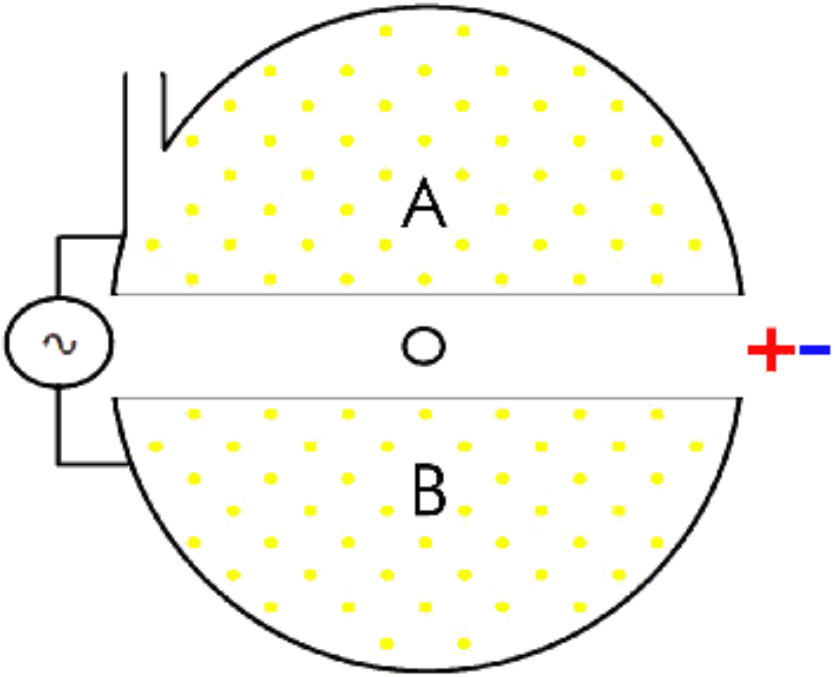
Isotope	Half-life (min)	$E_{max}(\beta^+)$ MeV	Production	Example tracer
^{11}C	20.4	0.96	$^{14}N(p,\alpha)^{11}C$	Methionine
^{13}N	9.96	1.19	$^{16}O(p,\alpha)^{13}N$	Ammonia
^{15}O	2.03	1.72	$^{15}N^*(p,n)^{15}O$ $^{14}N(d,n)^{15}O$	Water
^{18}F	109.7	0.635	$^{18}O^*(p,n)^{18}F$ $^{20}Ne(d,\alpha)^{18}F$	FDG (fluorodeoxyglucose)
^{62}Cu	9.7	2.93	^{62}Zn generator ($t_{1/2}$=9.2 hours)	PTSM (blood flow)
^{82}Rb	1.3	3.35	^{82}Sr generator ($t_{1/2}$=25 days)	Rb^+ (blood flow)
^{124}I	4.2 days	2.10	$^{126}Te(p,3n)^{124}I$	Labelled antibodies

Wide range of half-lives, generally shorter than conventional NM

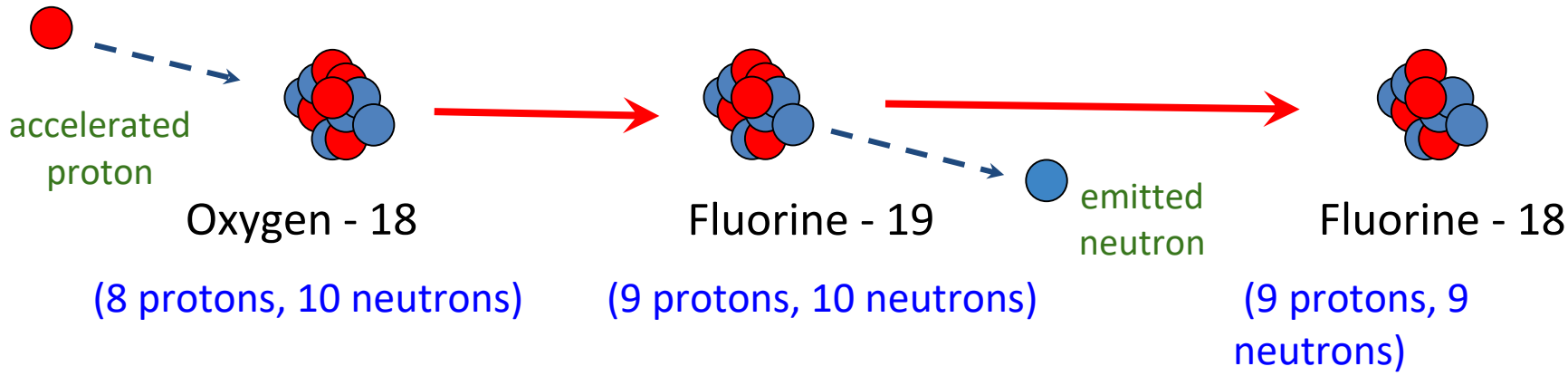
Mainly cyclotron produced but some generators

Physics of the Cyclotron

- Charged particle accelerator
  - particles fed into centre
- Alternating voltage
  - accelerates the particles
- Magnetic field
  - moves particles in a circle
  - more energetic spiral outwards
- Accelerated proton beam
  - used to make proton rich nucleii that decay by positron emission



How to make F-18

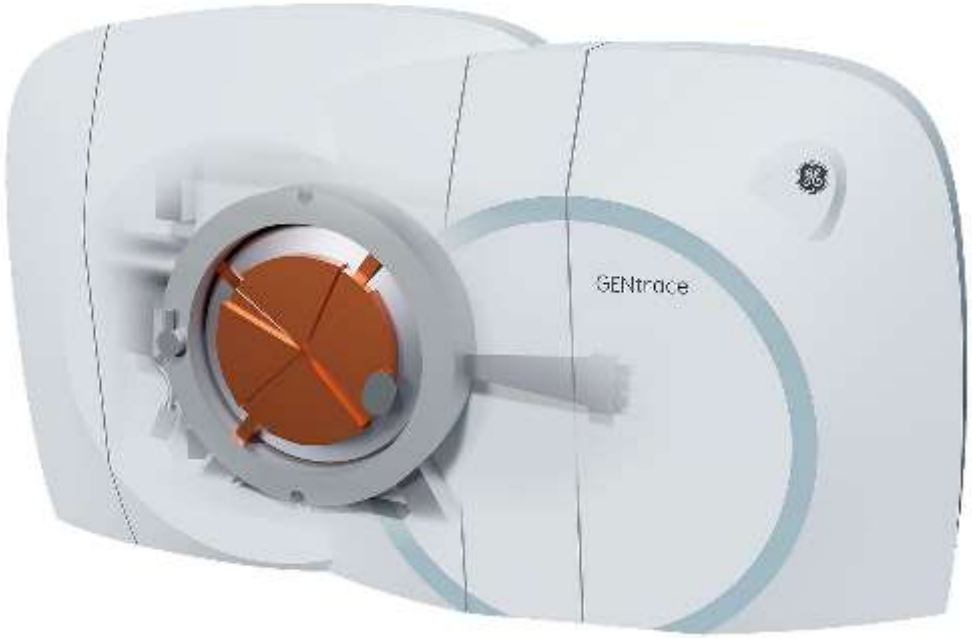


- proton irradiation of ^{18}O
- nucleus absorbs proton
- temporary creation of ^{19}F
- emission of a neutron
- production ^{18}F

- most common PET tracer FDG
- fluorodeoxyglucose
- trapped in metabolically active cells
- tracer agents increasing including PSMA, DOTATOC, florbetapir

The Cyclotron

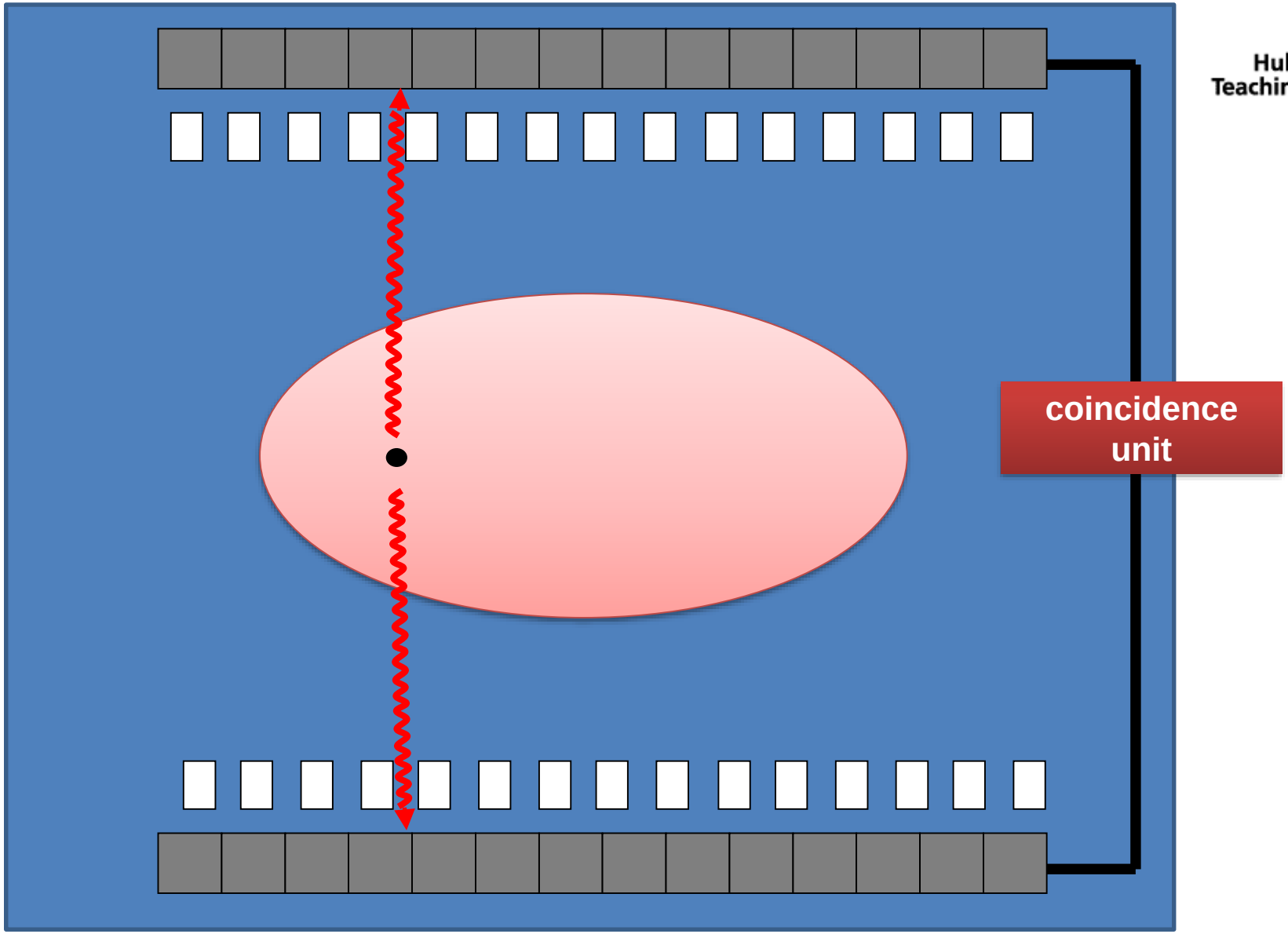
- GE GenTrace
- Produces F-18 and C-11
- 28GBq F-18 at 2 hour production
- 18.5GBq C-11 at 50 min production
- Weighs 49.6 metric tonnes
- Room size 5.8m x 6.2m x 2.5m

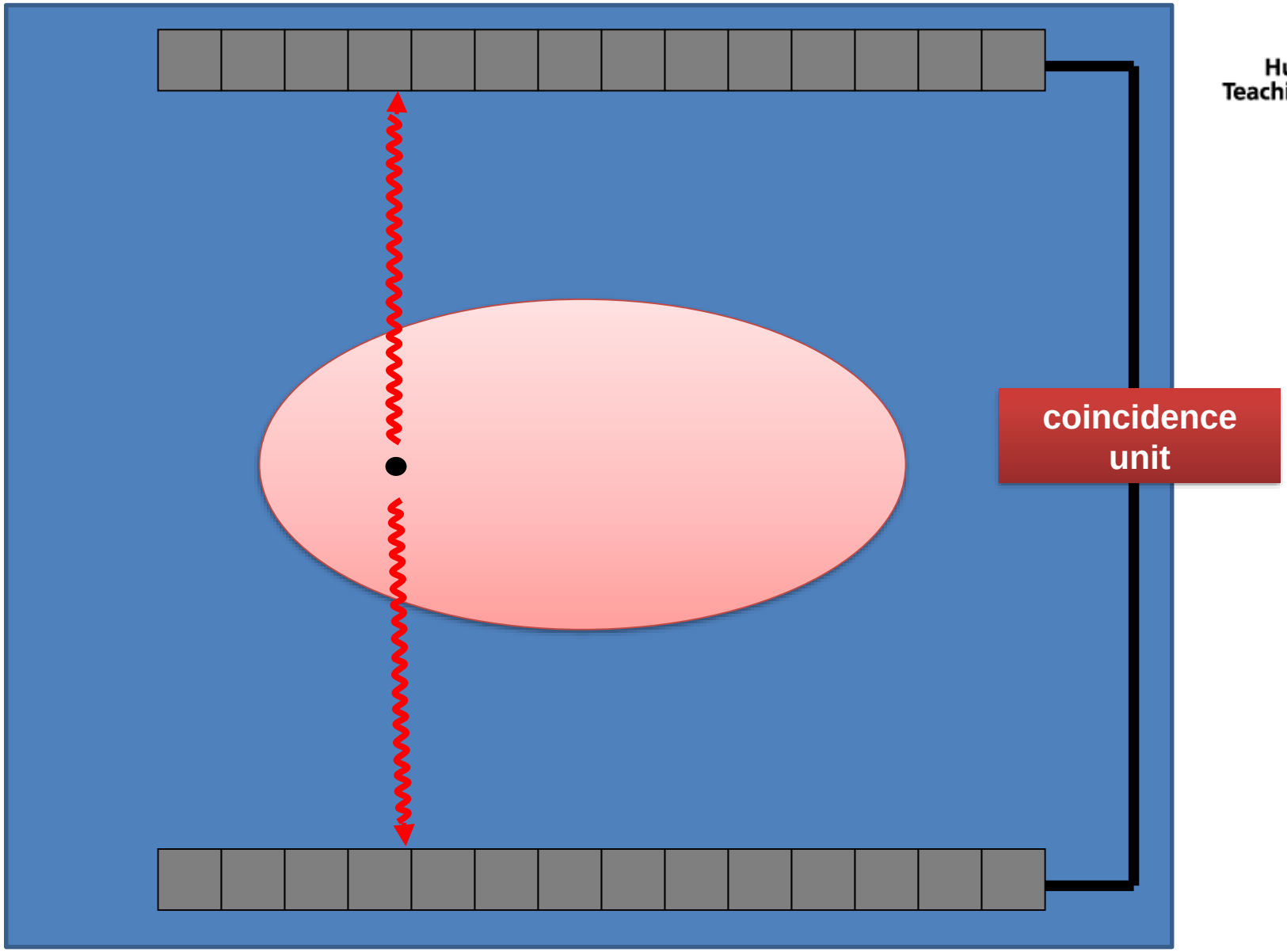


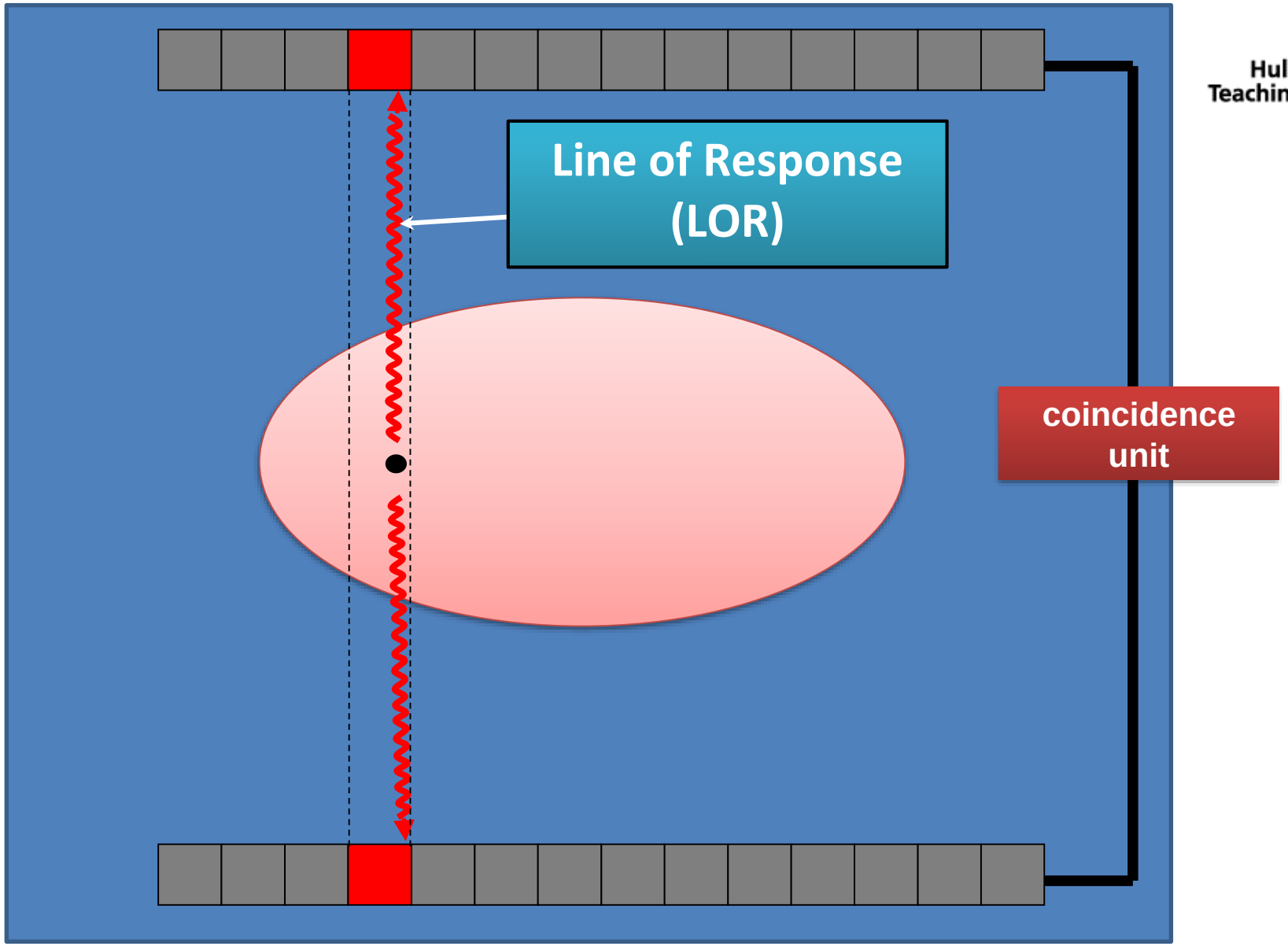
PET recap

- PET isotope properties and production
- positron + electron = 511 keV annihilation photons
- PET imaging - detect and locate origin of annihilation photons

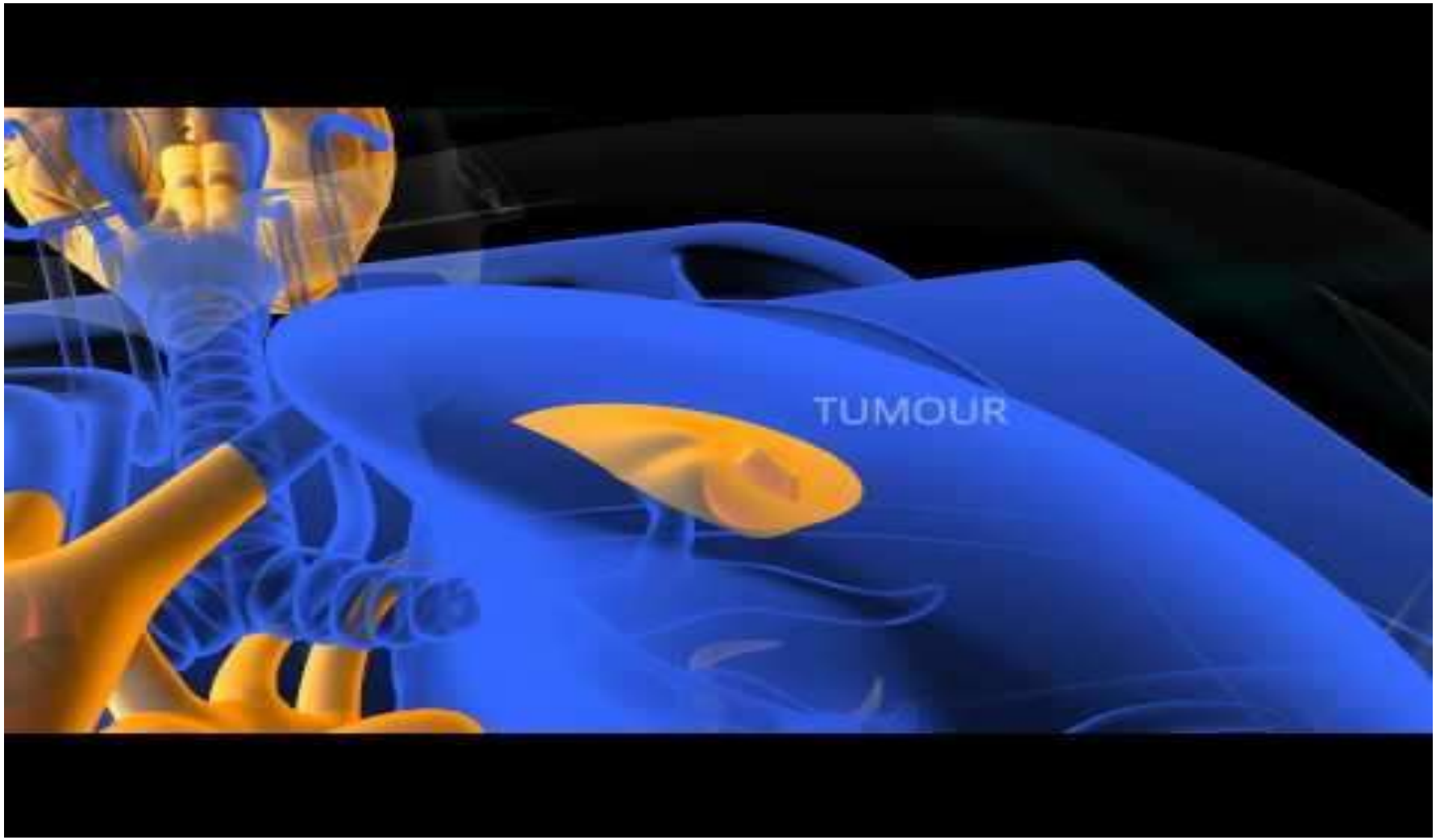



coincidence unit


coincidence
unit


Line of Response
(LOR)
coincidence
unit

PET imaging



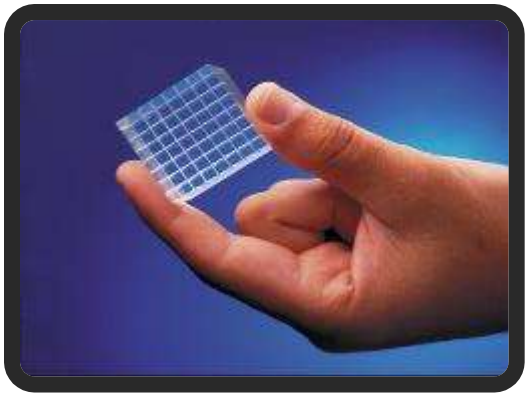
Scintillator Crystals

Crystal	Relative Light Output (%)	Decay Time (ns)	Density (g/cm^3)	Effective Atomic Number (Z)	Energy Resolution at 511 keV (%)
NaI(Tl)	100	230	3.7	51	7.8
BGO	15	300	7.1	75	10.1
LSO	75	40	7.4	65	10.0
GSO	35	60	6.7	59	9.5

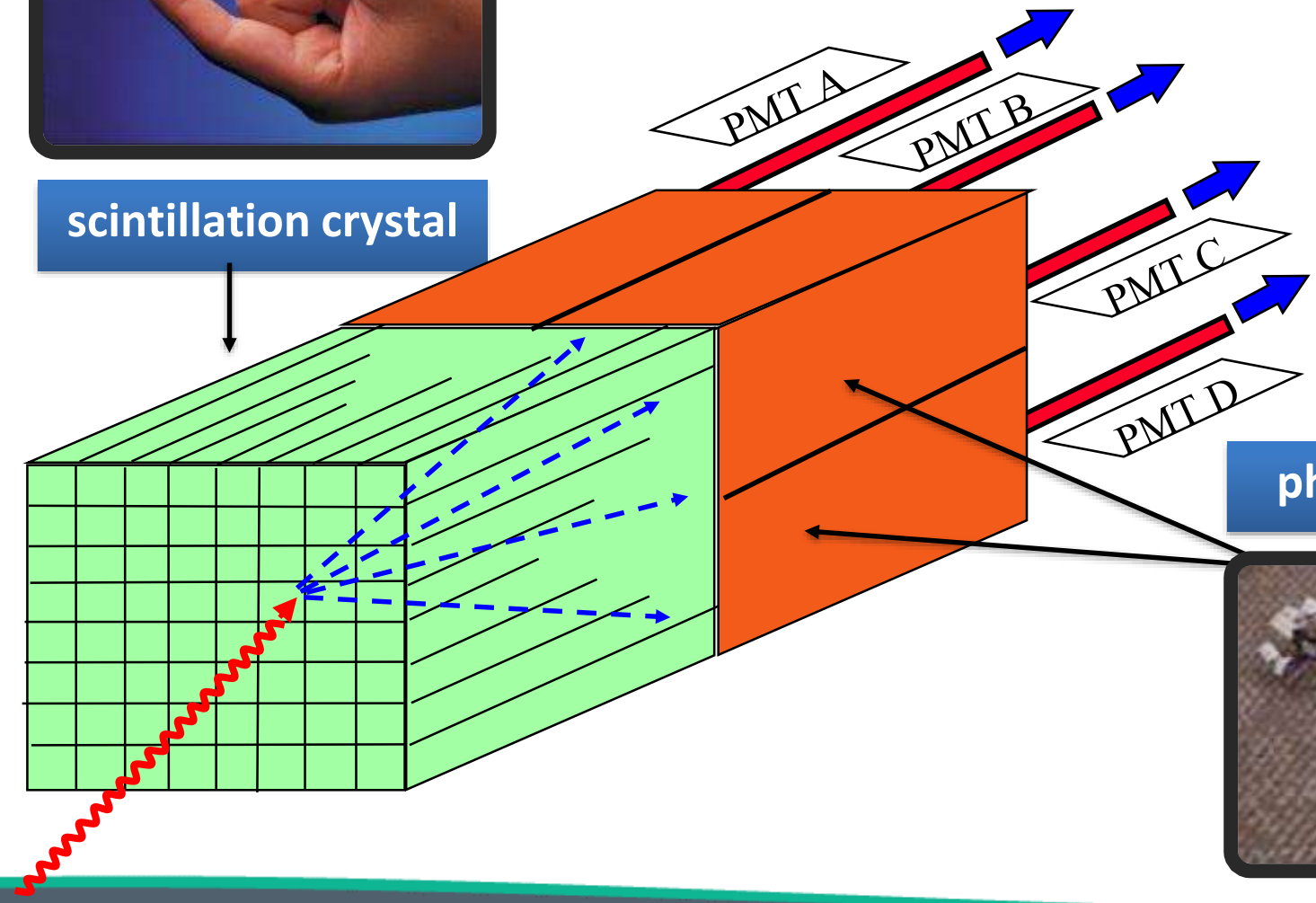
Ideal scintillator

- available, cheap, easy to make
- high detection efficiency
- short scintillation decay time
- good energy resolution

PET Detector Block



scintillation crystal

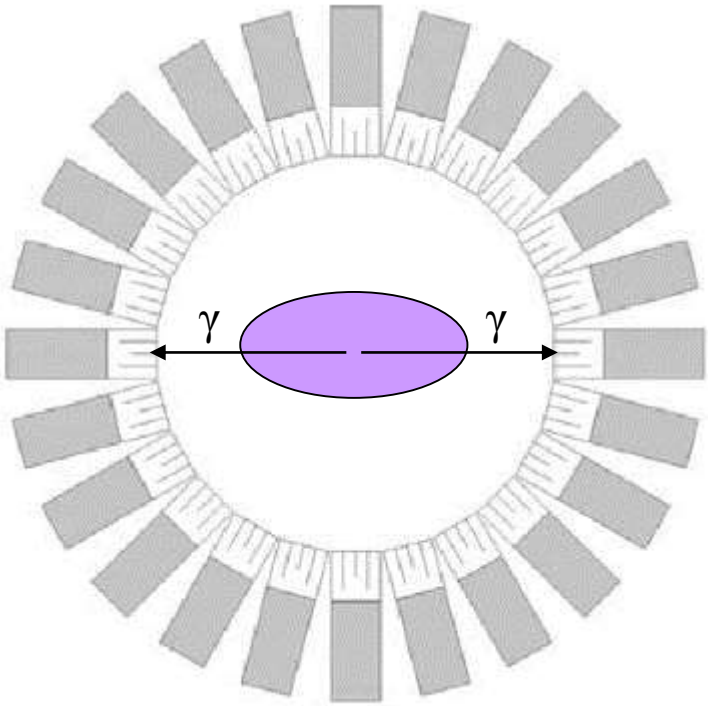


PMT output -->
- amplification
- digitisation
- energy discrimination

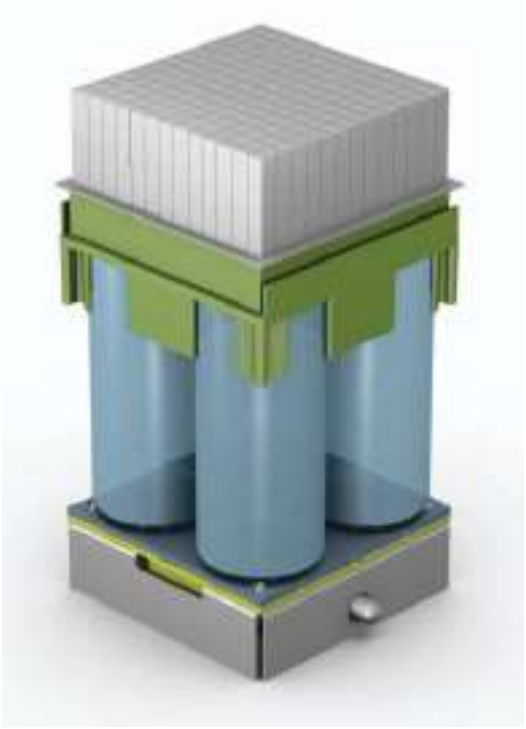
photomultipliers



PET Crystal Array



Annular Detector Array



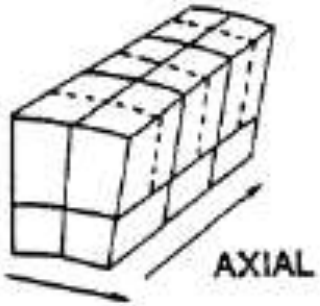
Detector Block

PET Detector Ring

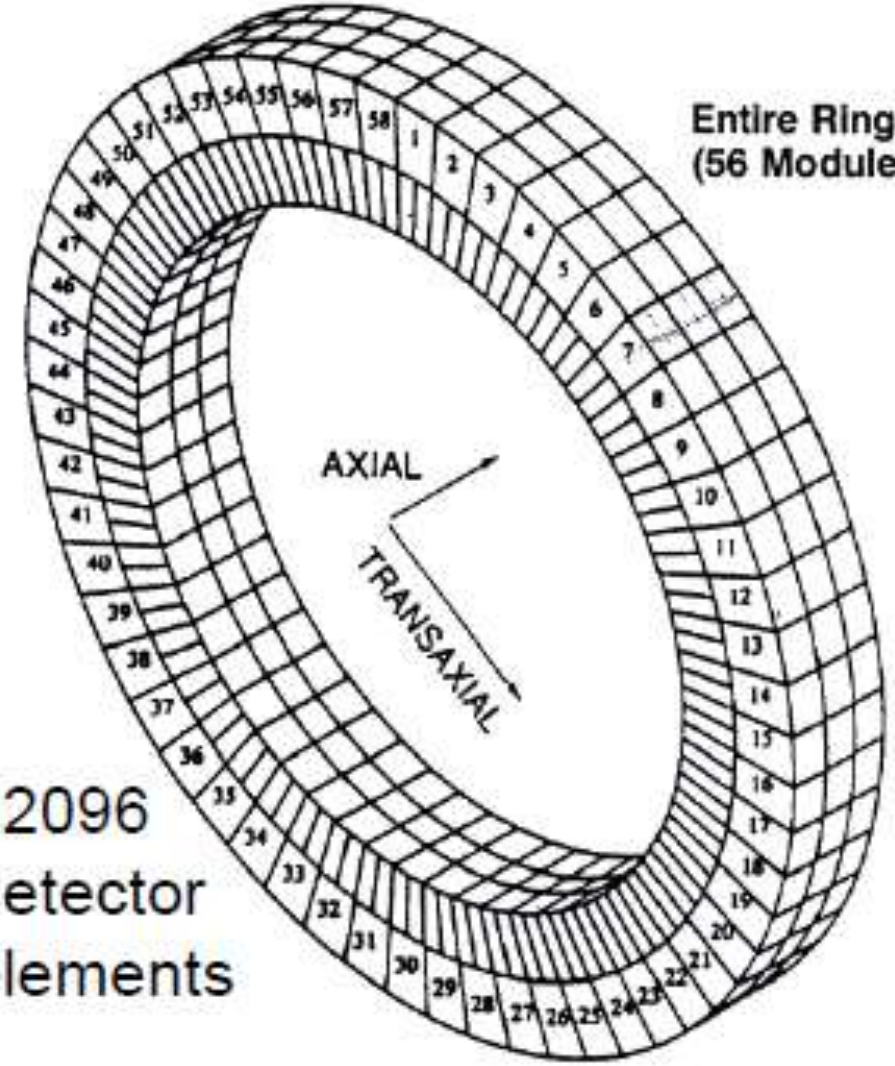
Block (6 x 6 block of BGO crystals)



Module (6 Blocks)

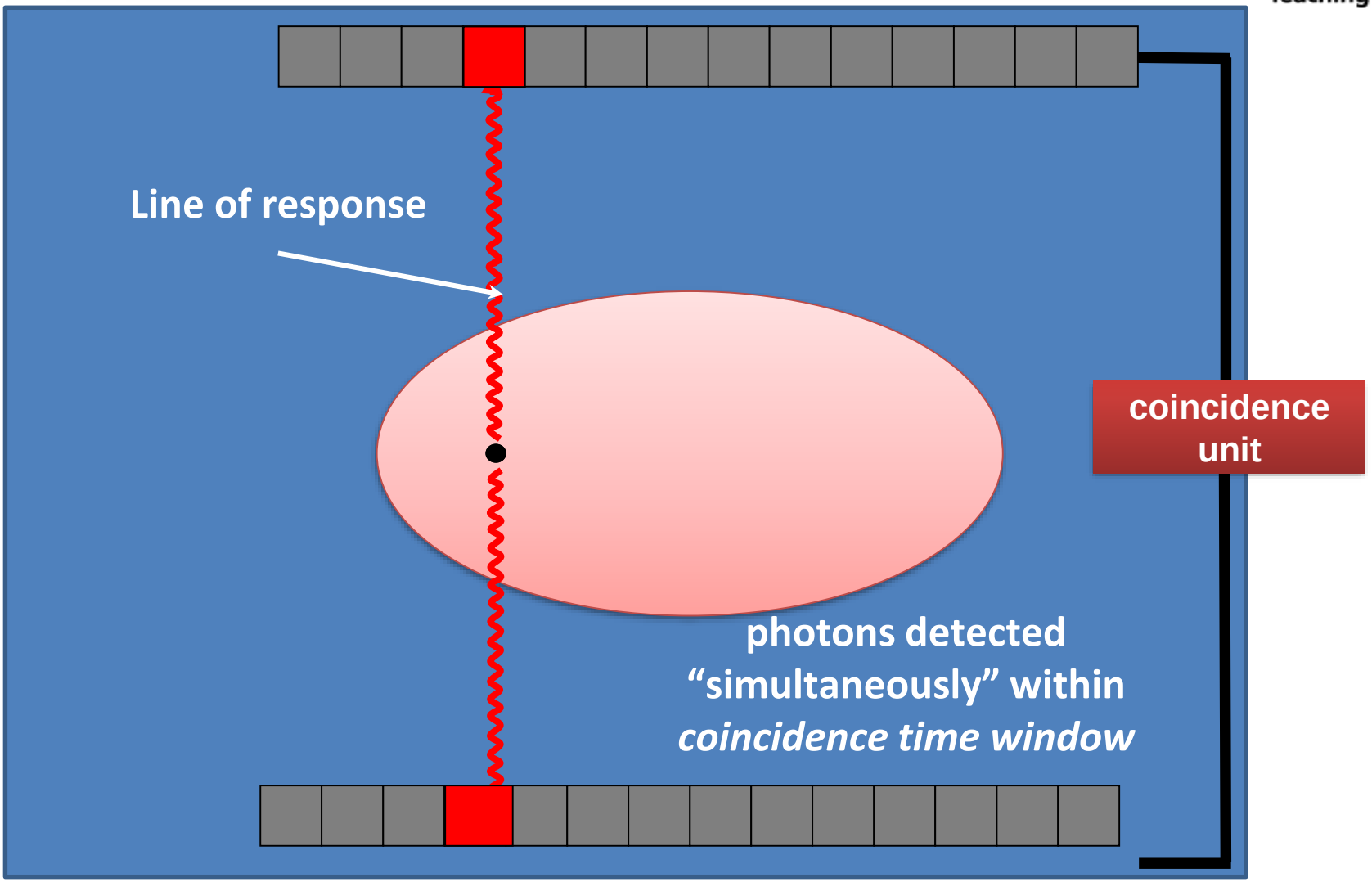


Entire Ring (56 Modules)



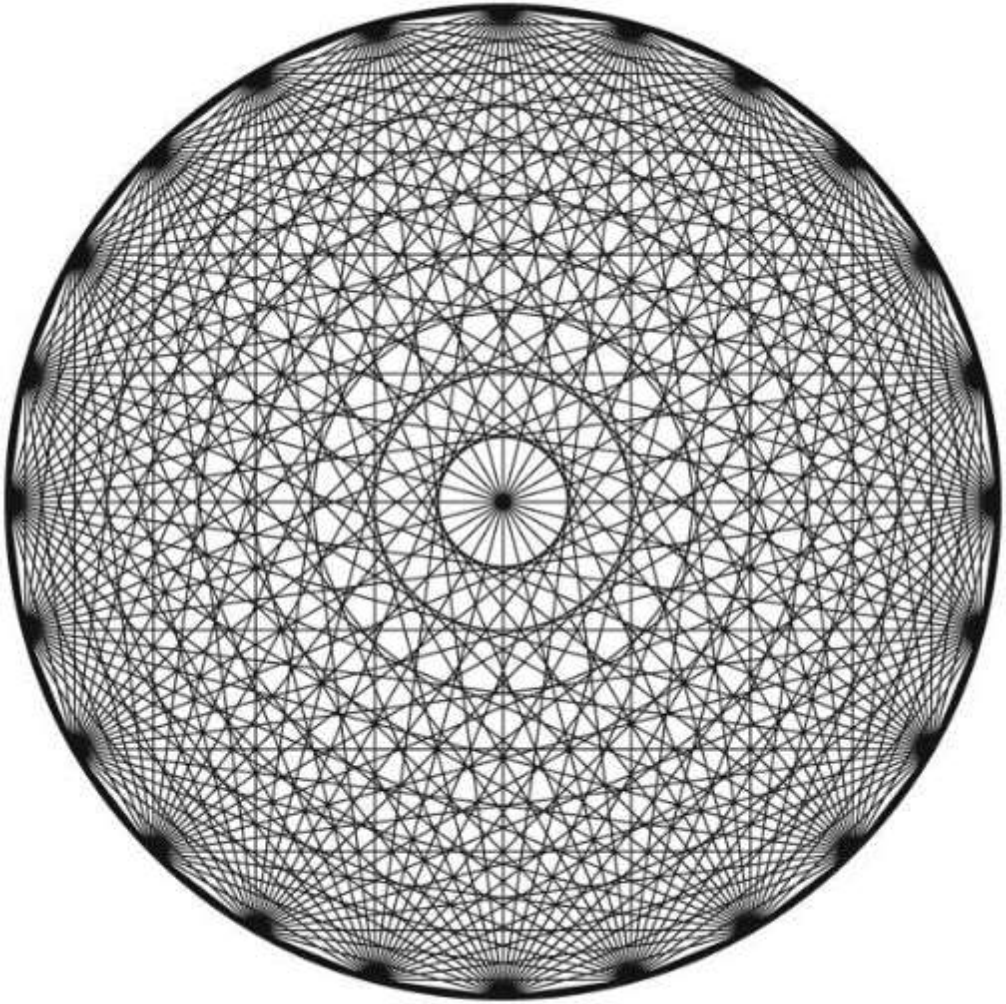
12096 detector elements

True Coincidence Event

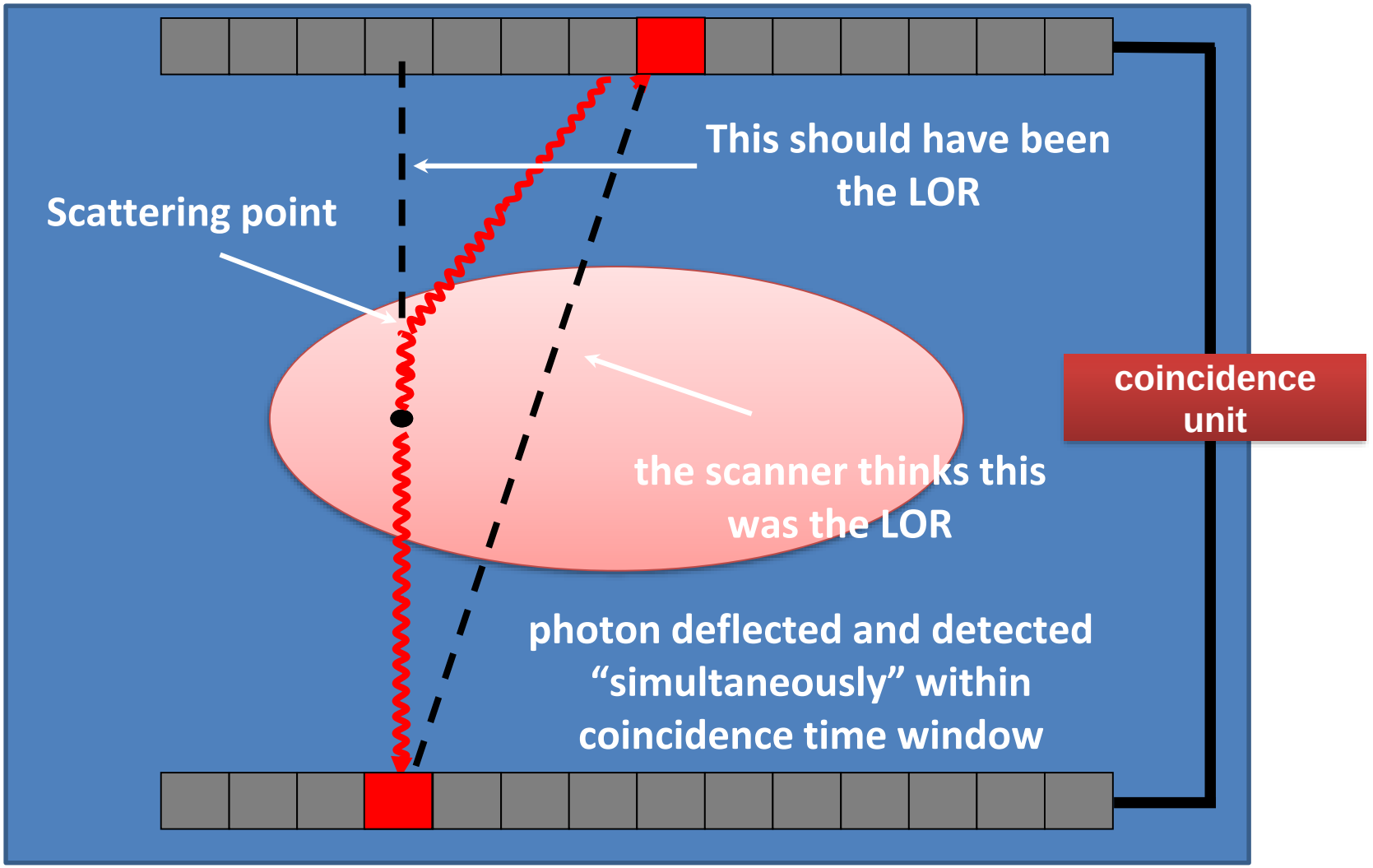


Annular LOR's

- Coincidence detection
- Large number of LOR's
- Sampling depends on position in FOV



Scatter Coincidence Event



Random Coincidence Event

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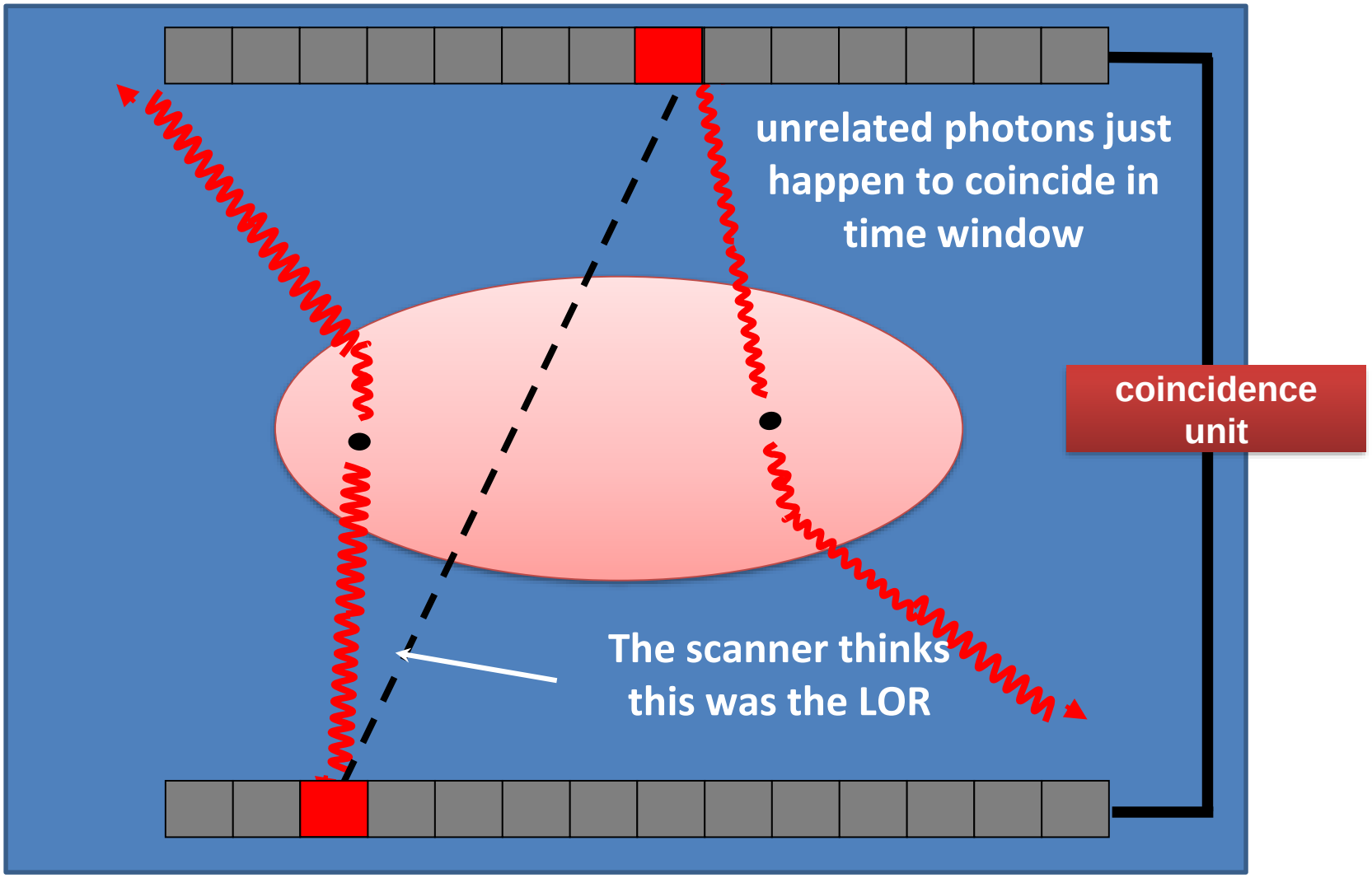
Hull University Teaching Hospitals
NHS Trust



Remarkable people.
Extraordinary place.

PET Image Creation

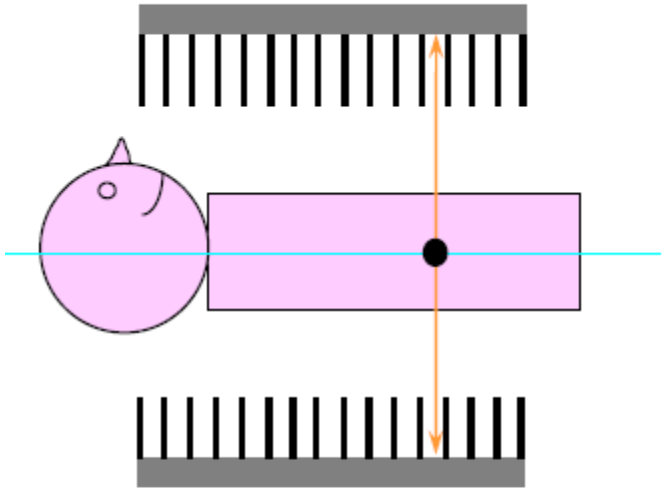
- Reduction of random and scatter effects
- Axial FOV - width of annular rings
- Data summed along each LOR
- Plotted as a function of angle and distance from the centre of the scanner
- Coincidence events analysed
- Projection views produced



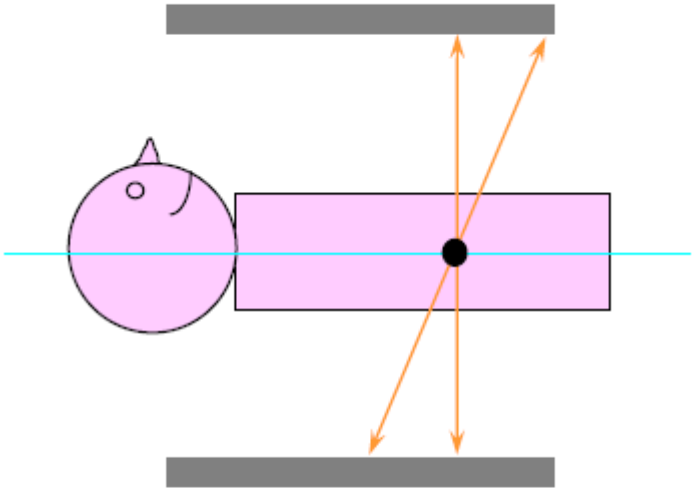
Acquisition Modes

NHS
Hull University Teaching Hospitals
NHS Trust

- **2D**



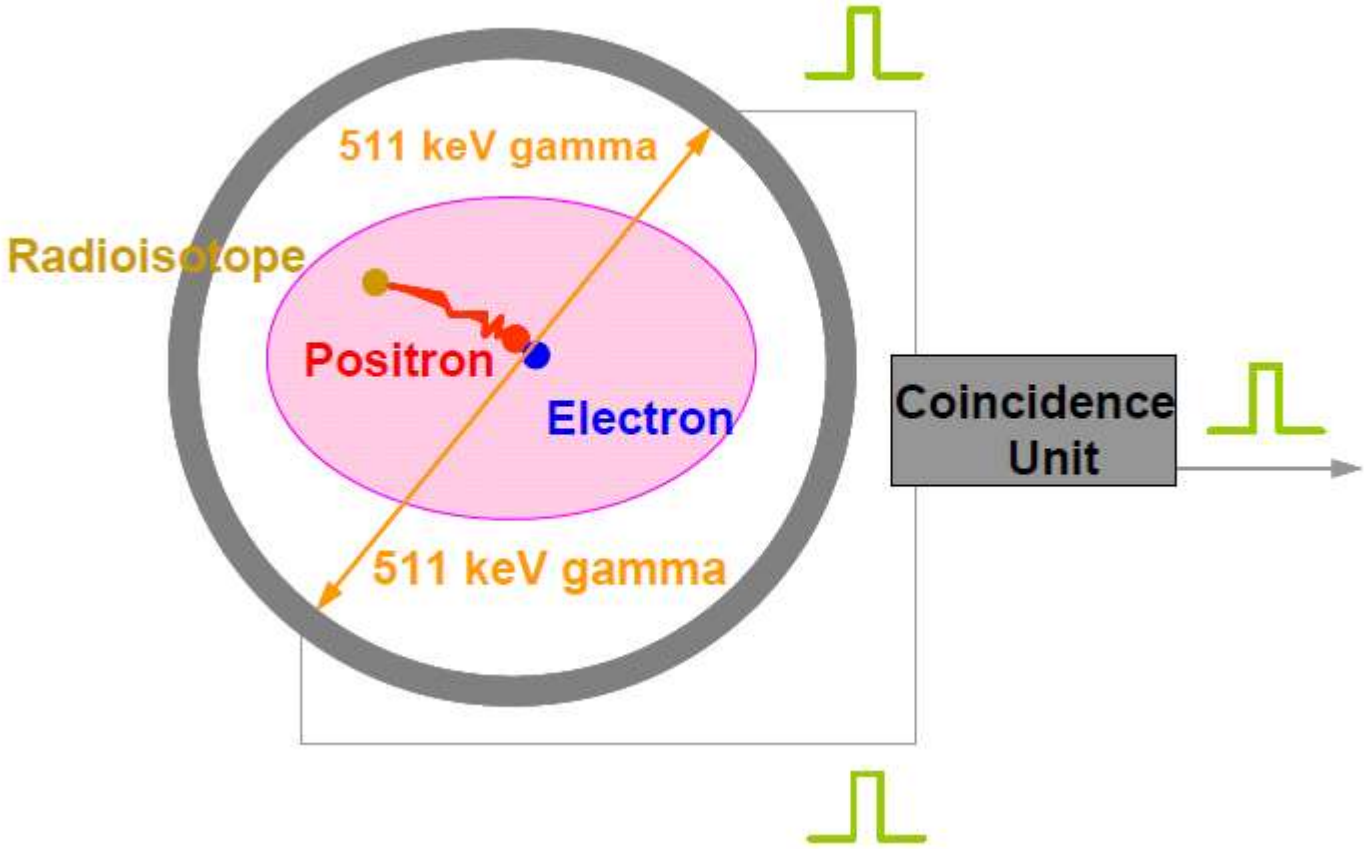
- **3D**



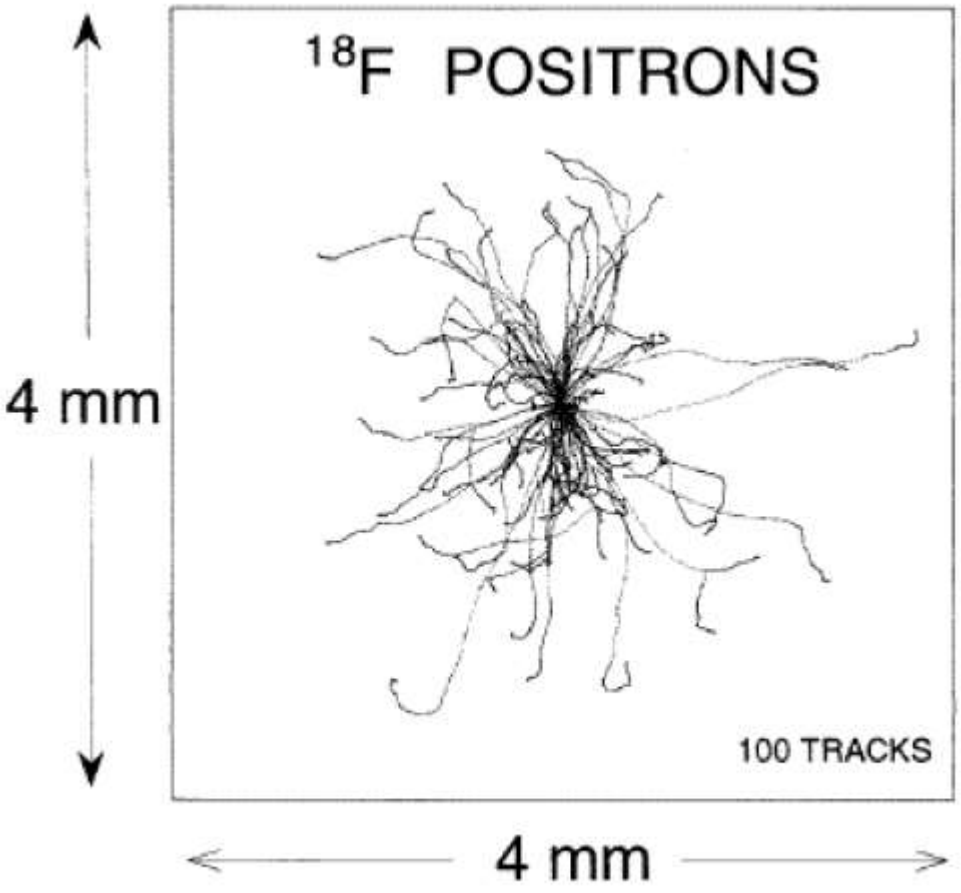
- Less randoms and scatter, but reduced sensitivity
- Highest sensitivity but high randoms and scatter

Remarkable people.
Extraordinary place.

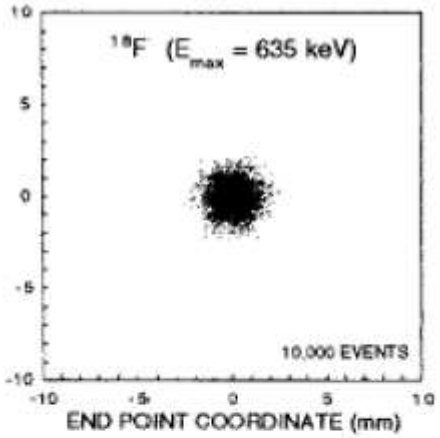
It’s not as simple as that !

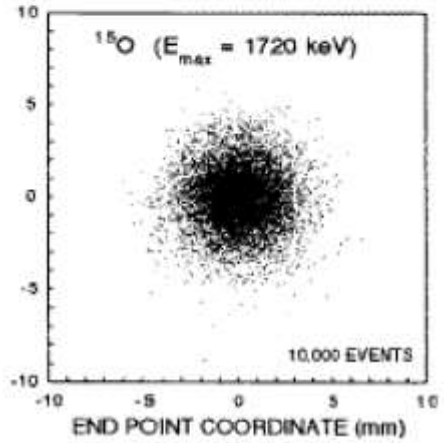


Physical Limits on Resolution



Simulated ^{18}F positron tracks from a point source in water.





from Levin & Hoffman PMB 1999; 46:781-799

Variation of Resolution with Positron Energy

Isotope	Half-life (min)	$E_{max}(\beta^+)$ MeV	Production	Example tracer
^{11}C	20.4	0.96	$^{14}N(p,\alpha)^{11}C$	Methionine
^{13}N	9.96	1.19	$^{16}O(p,\alpha)^{13}N$	Ammonia
^{15}O	2.03	1.72	$^{15}N^*(p,n)^{15}O$ $^{14}N(d,n)^{15}O$	Water
^{18}F	109.7	0.635	$^{18}O^*(p,n)^{18}F$ $^{20}Ne(d,\alpha)^{18}F$	FDG (fluorodeoxyglucose)
^{62}Cu	9.7	2.93	^{62}Zn generator ($t_{1/2}$=9.2 hours)	PTSM (blood flow)
^{82}Rb	1.3	3.35	^{82}Sr generator ($t_{1/2}$=25 days)	Rb^- (blood flow)
^{124}I	4.2 days	2.10	$^{126}Te(p,3n)^{124}I$	Labelled antibodies

(*=enriched target)

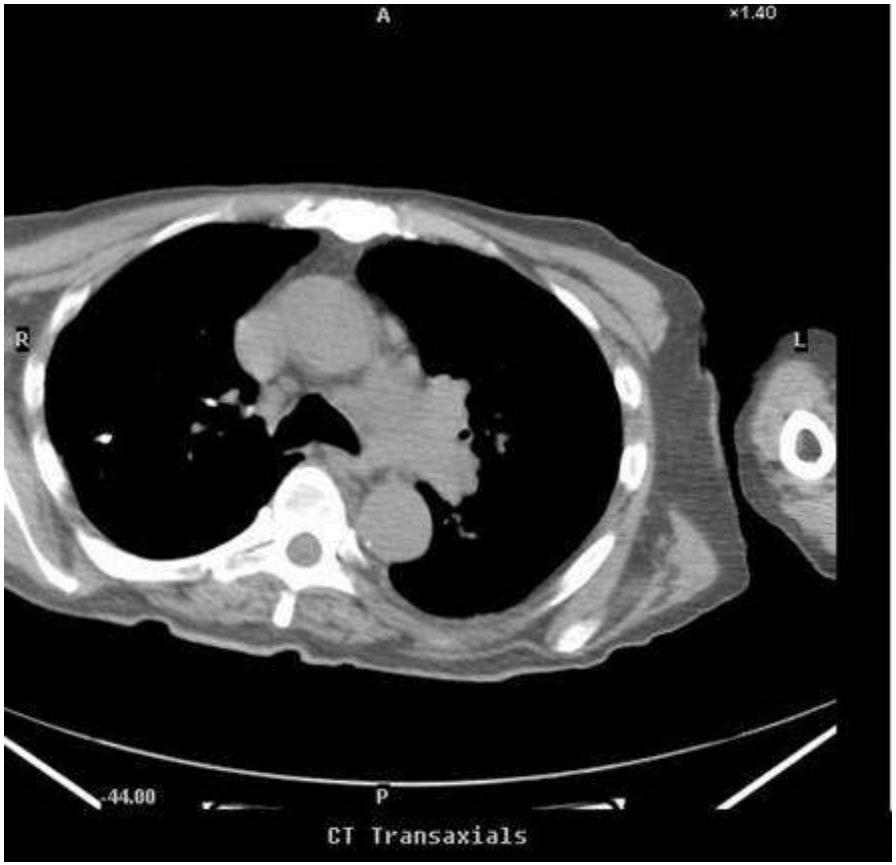
Wide range of positron energies

higher energy → worse spatial resolution

Imaging Modality Resolution Comparison

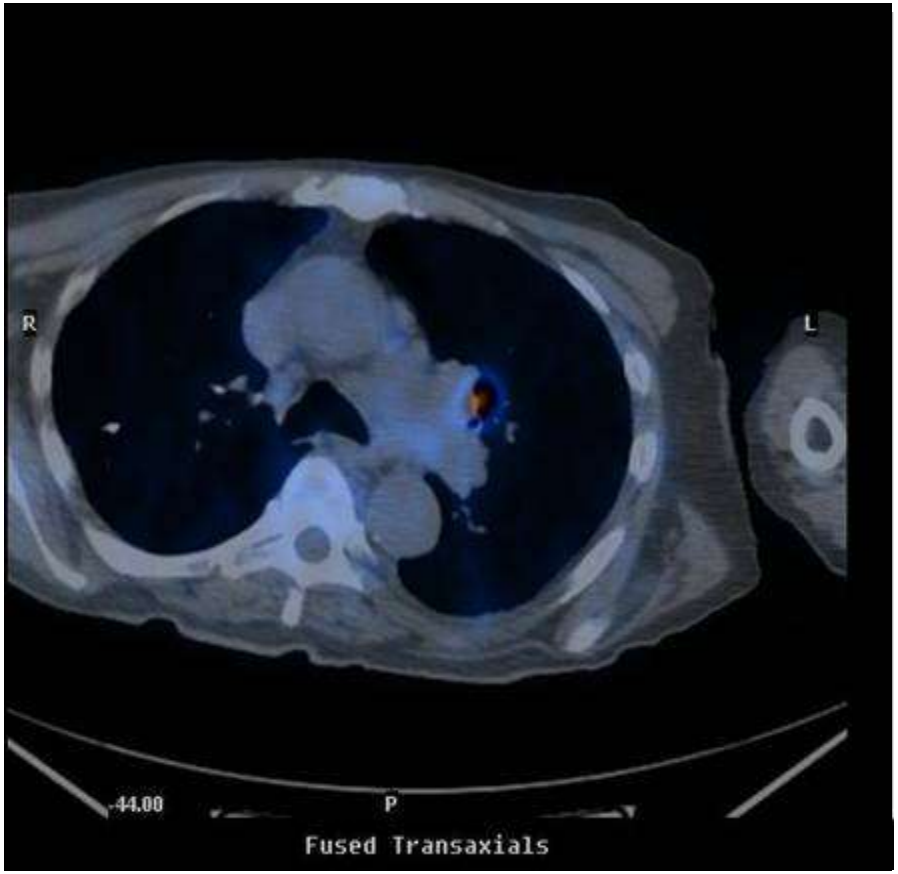
Nuclear Medicine	6 to 8 mm
PET	2 to 3 mm
MRI	0.5 to 2 mm
CT	0.5 to 1 mm
Mammography	0.1 to 0.5 mm

CT



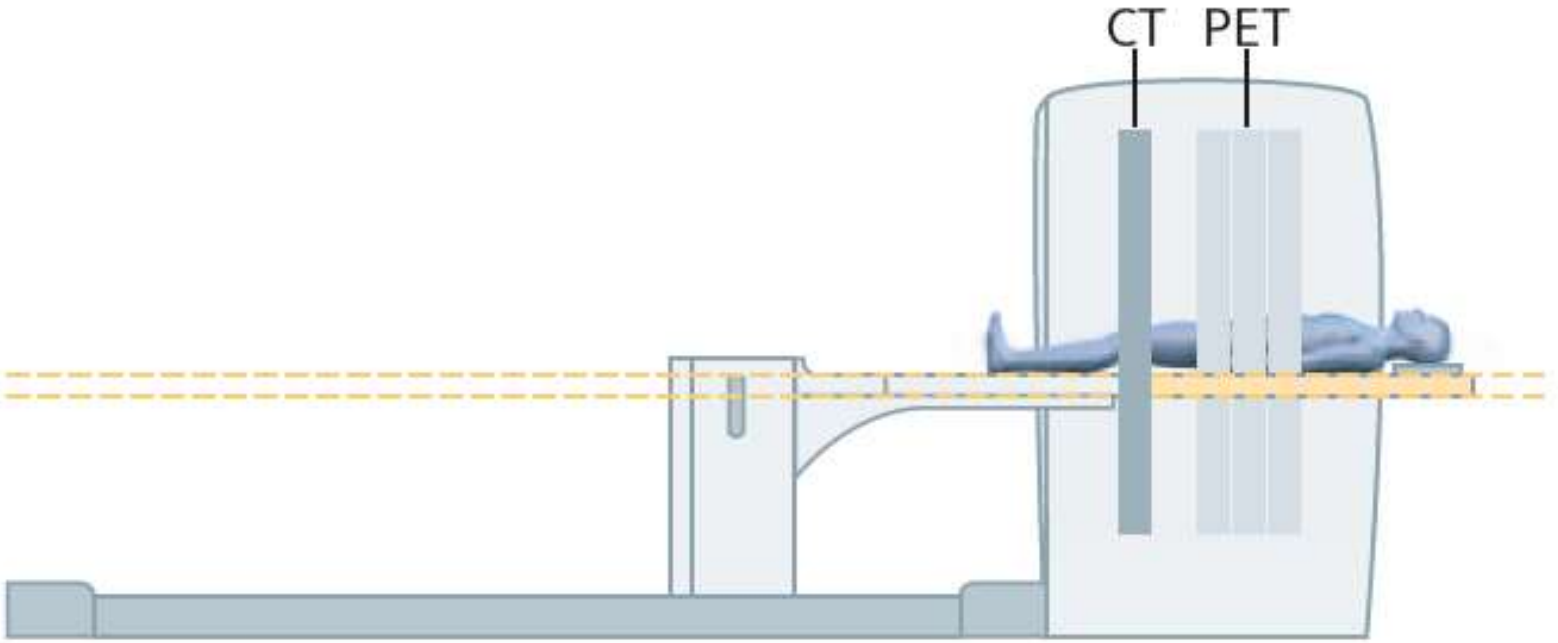
- Anatomical detail
- Better resolution than PET
- Cannot differentiate biologically active and inactive cells

PET/CT



- Combines function with anatomy
- Accurate anatomical registration
- Higher diagnostic accuracy than PET or CT alone

Current PET ≈ PETCT



Current PET ≈ PETCT

GE MEDICAL SYSTEMS



Discovery
ST
STE
VCT
STE RX
VCT RX
600
690

PHILIPS



Gemini GXL
Gemini TF

SIEMENS

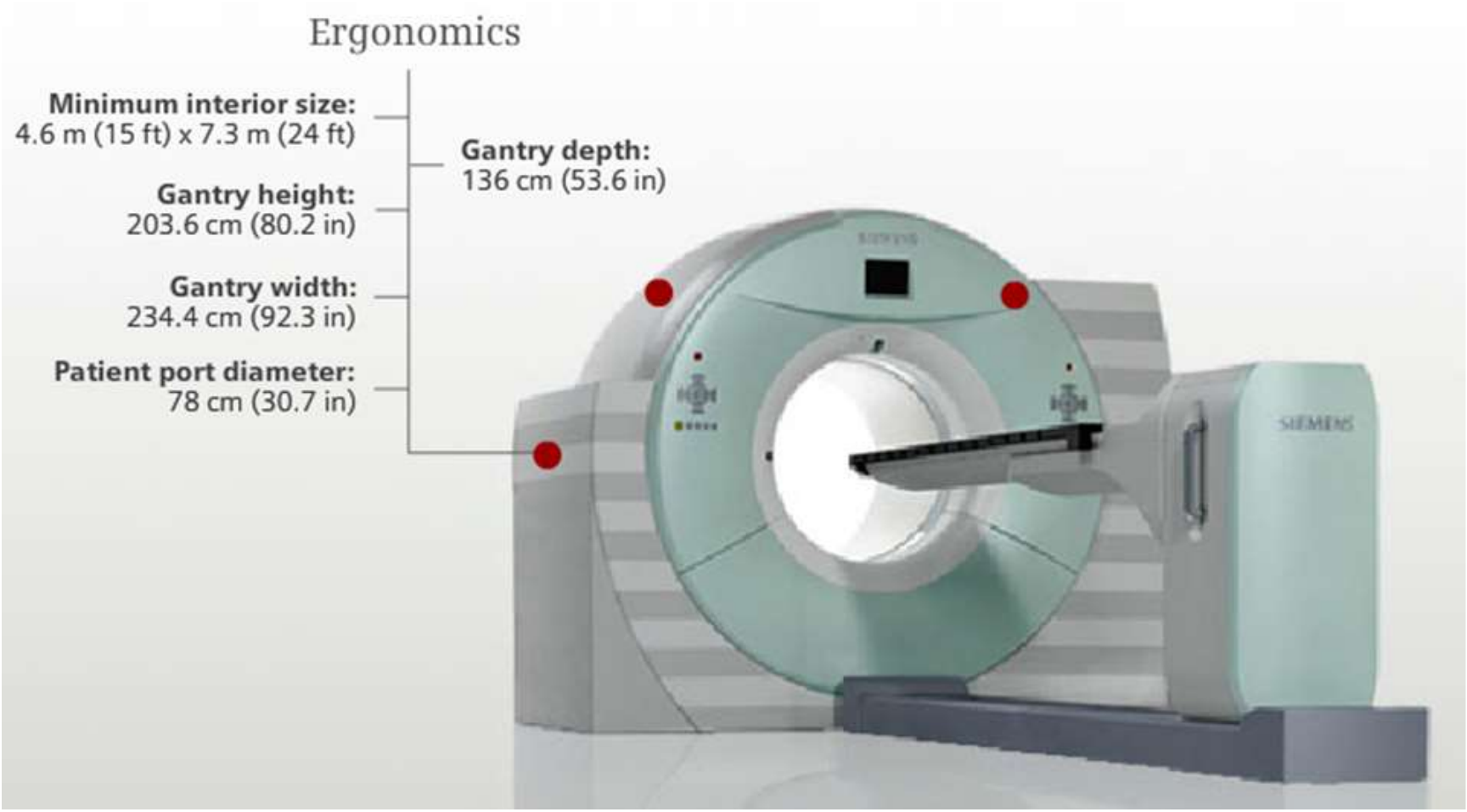


Biograph



mCT

Siemens Biograph mCT



Covers off

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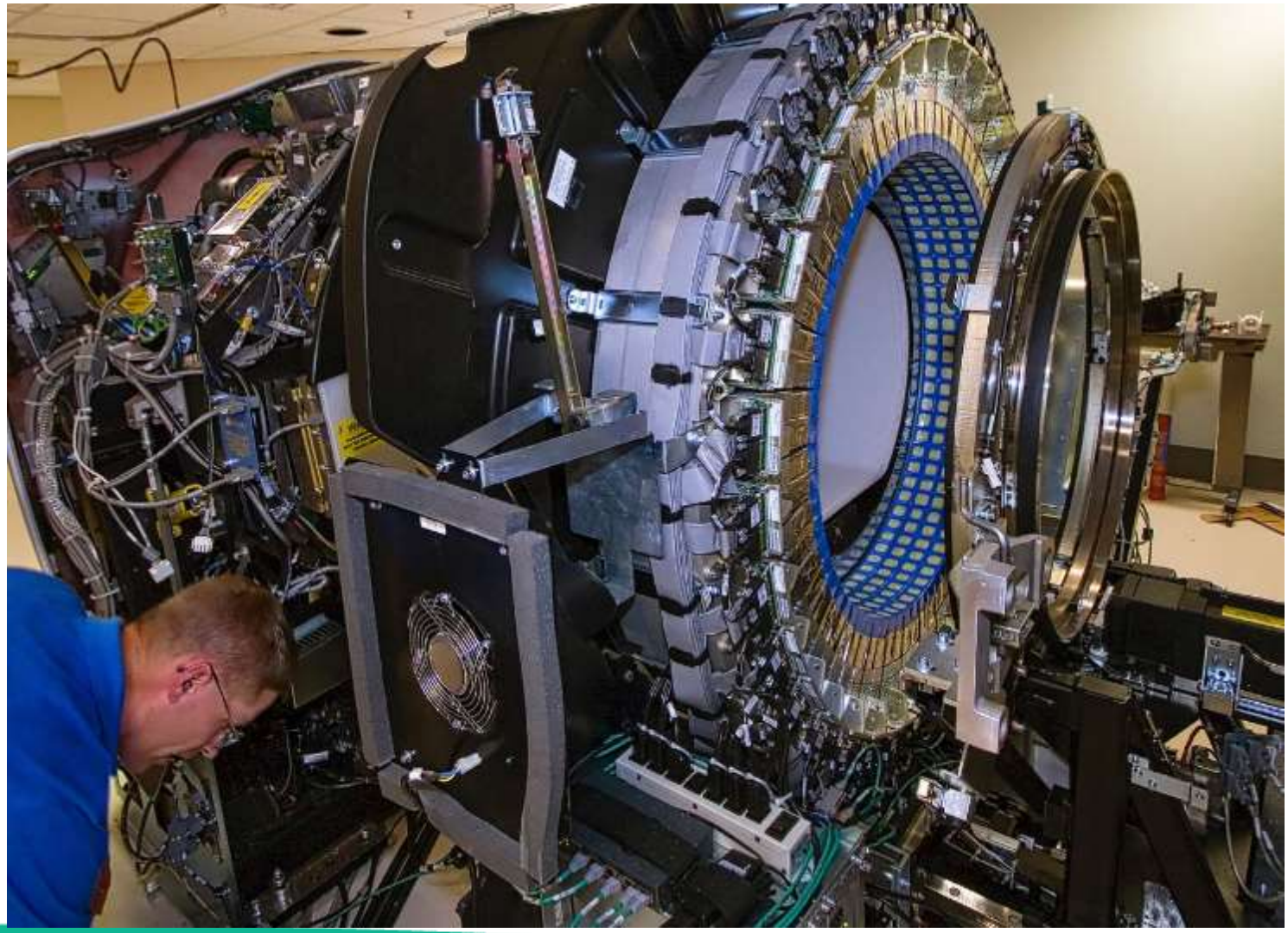
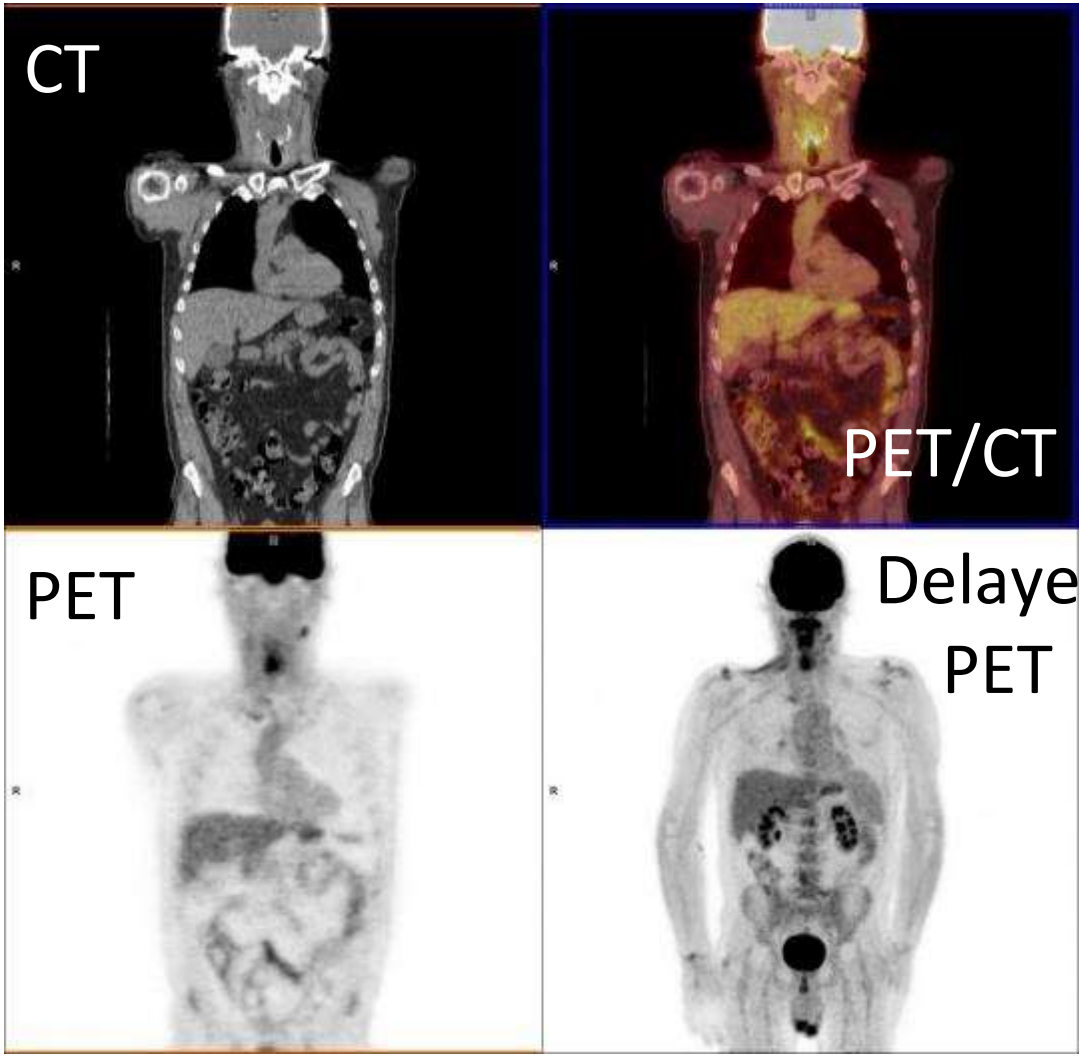
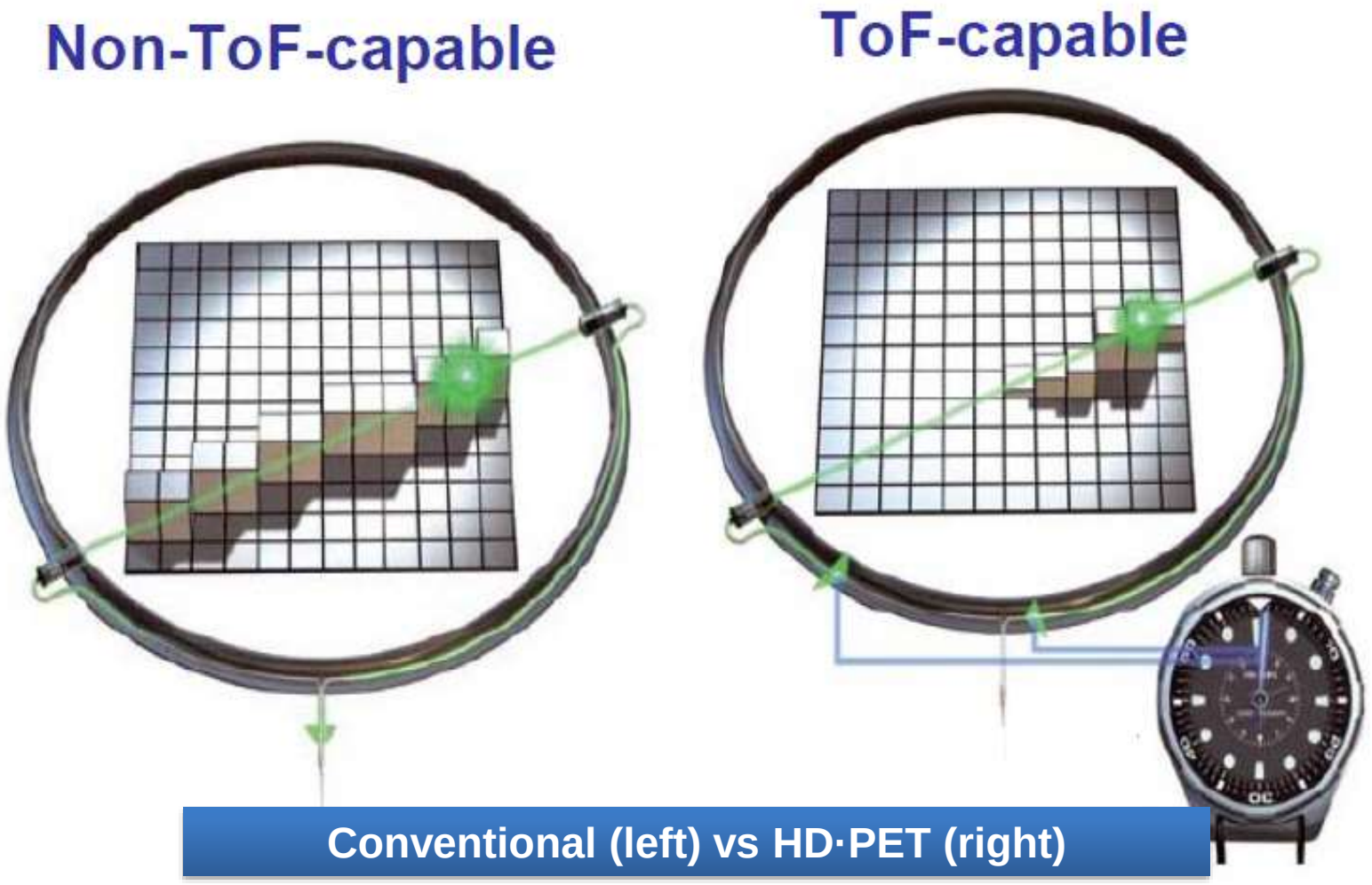
NHS Trust



PET/CT Image Recon



“Time-of-Flight” (TOF)

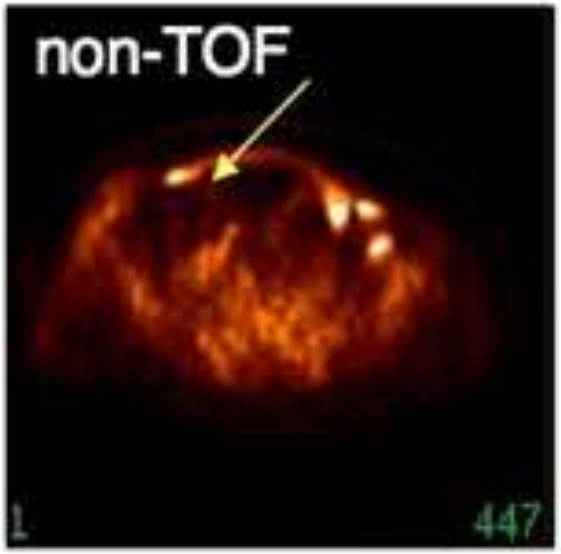


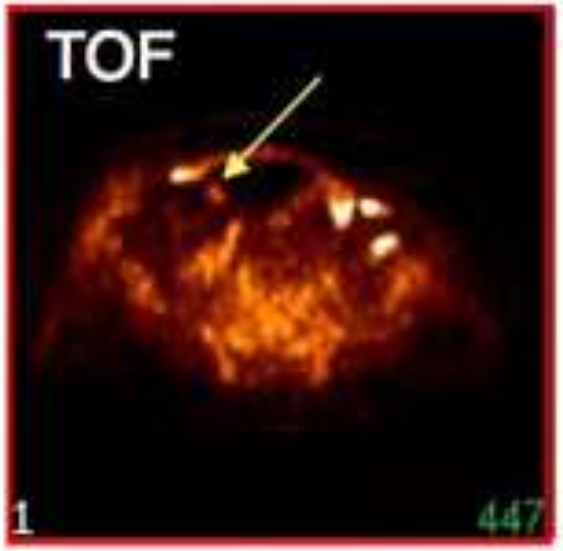
Conventional (left) vs HD·PET (right)

Improved Contrast with (TOF)

Hull University Teaching Hospitals NHS Trust







Standardised Uptake Value (SUV)

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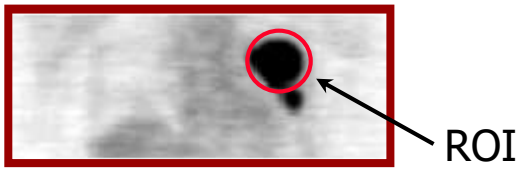
Semi quantitative analysis based on

- region of interest values
- applying activity (kBq/ml) in the region of interest to patient weight and dose

$$SUV = \frac{Uptake\ (\frac{kBq}{ml})}{activity\ (MBq)/weight(kg)}$$



before chemotherapy
SUV = 17.2



chemotherapy day 7
SUV = 3.9



chemotherapy day 42
SUV = 1.8

The Warburg effect

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Normal cell + oxygen → glucose conversion → carbon dioxide

Tumour cells + oxygen → increased glucose conversion → lactate

Hypoxia

‘the propensity for tumours
to metabolise glucose <u>anaerobically</u>
even when oxygen is available’

Basis for PET is
increased glucose uptake in tumour cells.
Higher concentrations
in some malignant cancers

FDG PET only one part of cellular metabolism
Other pathways and alternative cell fuels

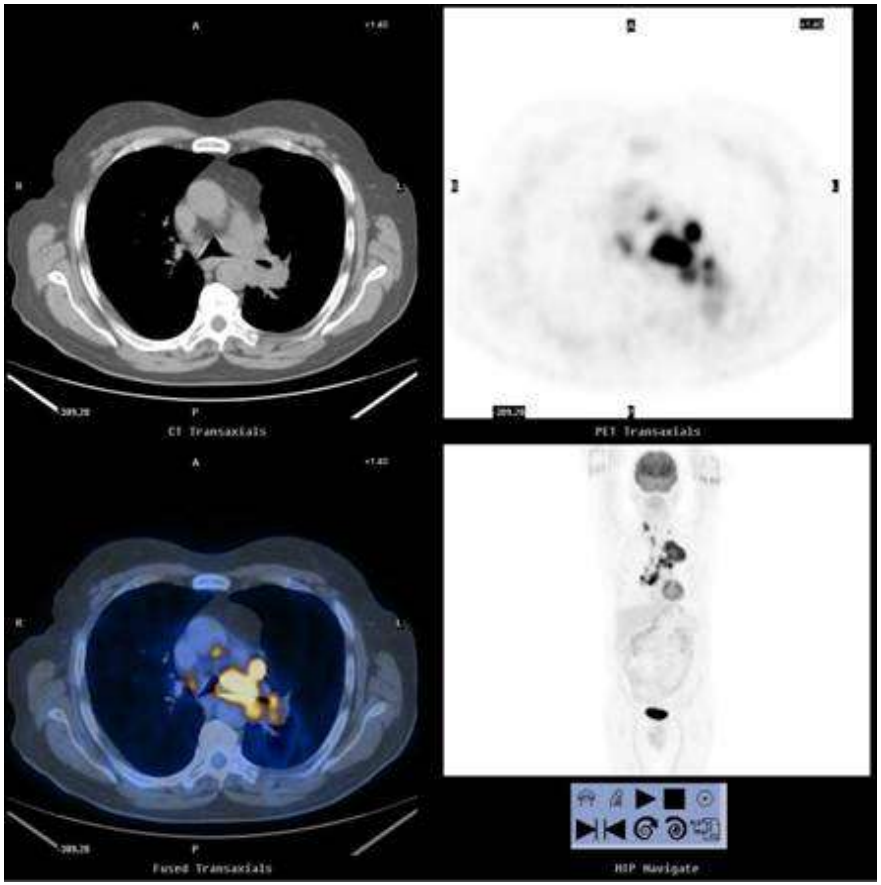
Why proliferating cells exhibit the Warburg effect is not fully understood

Pantel AR *et al.* Imaging Cancer Metabolism: Underlying Biology and Emerging Strategies. J Nucl Med. 2018 vol.59 no.9 **1340-1349**

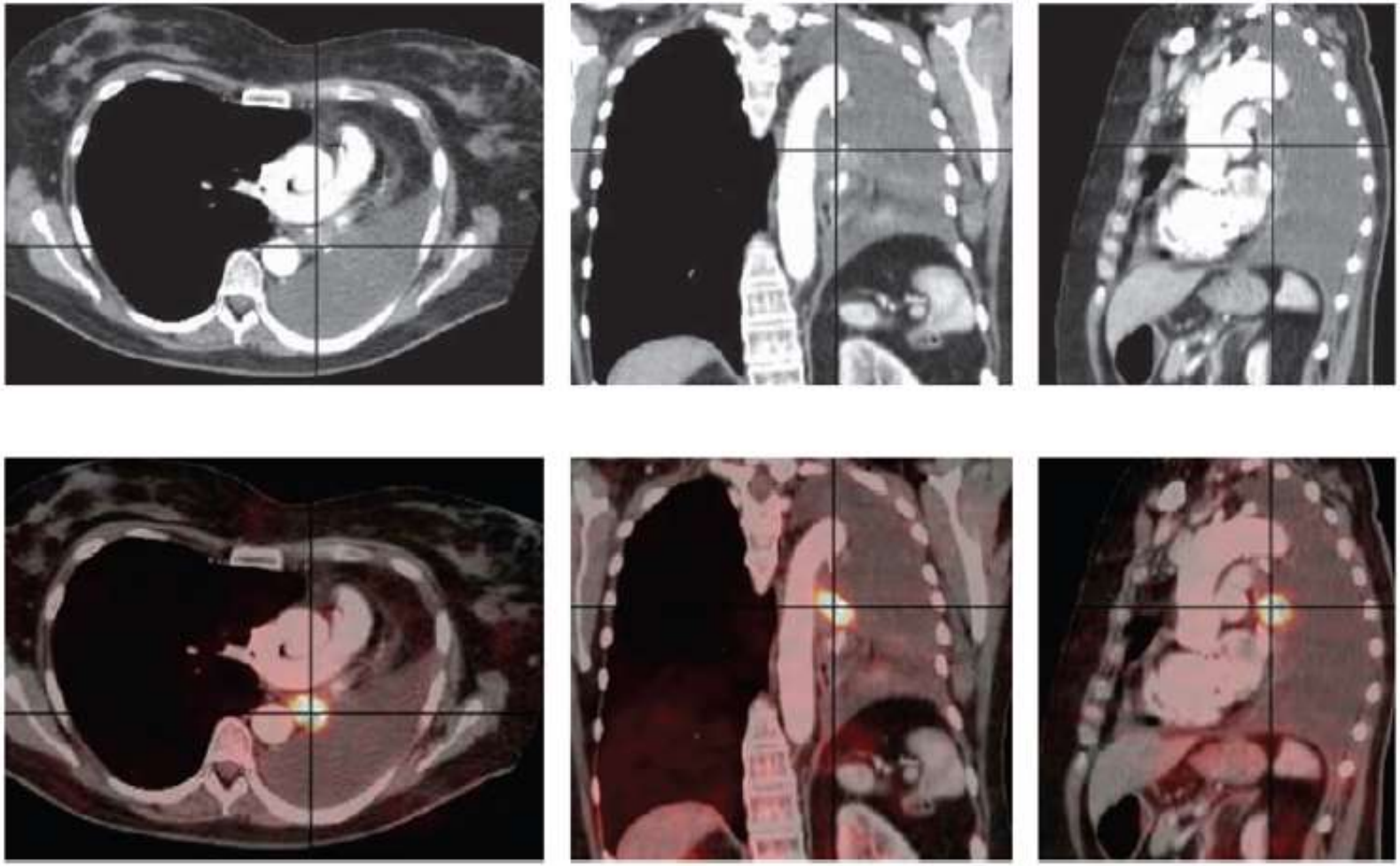
PET Applications
Oncology

Role in Oncology

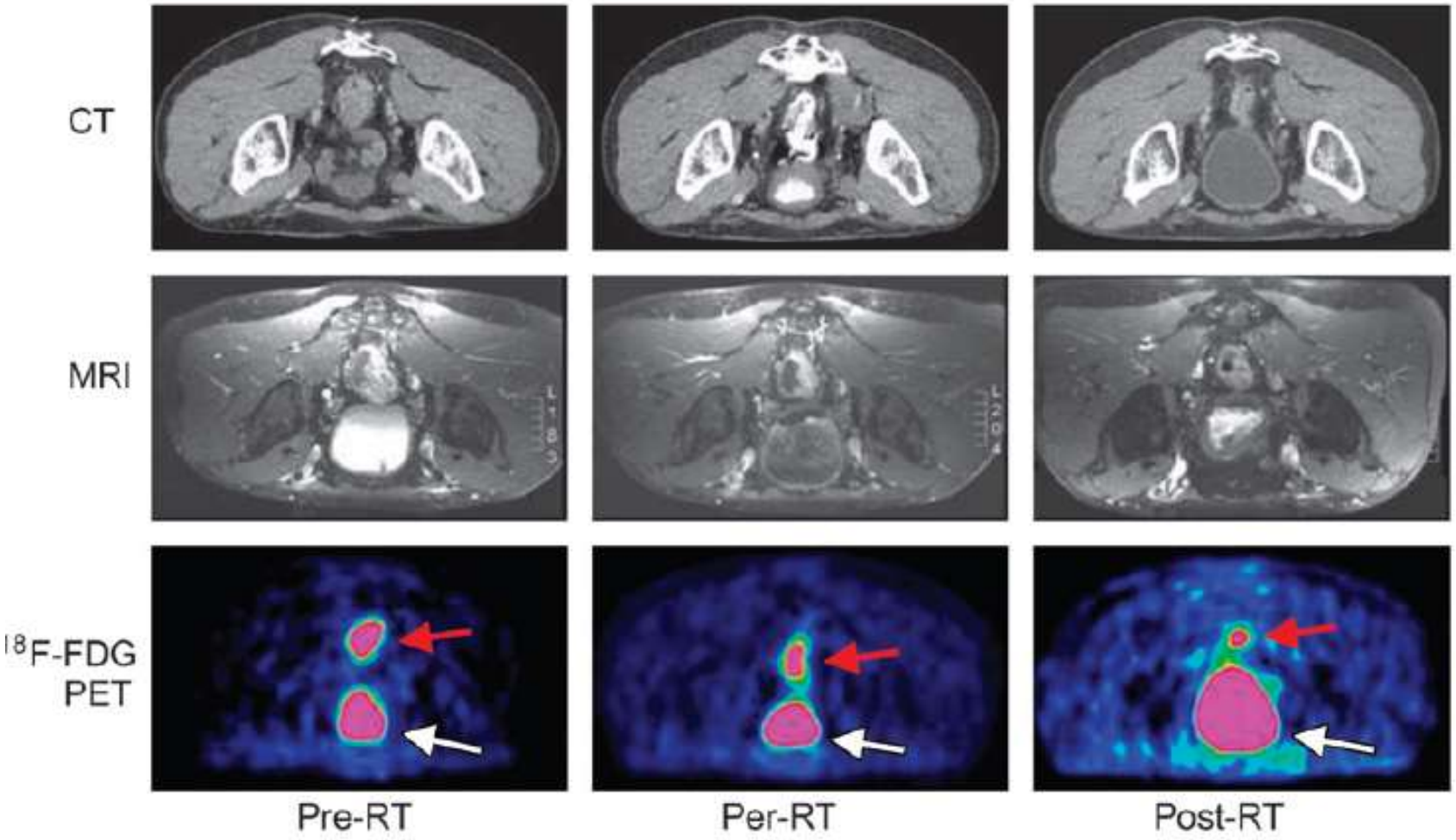
- Differentiate benign from malignant disease
- Staging of disease
- Treatment response
- Radiotherapy treatment planning



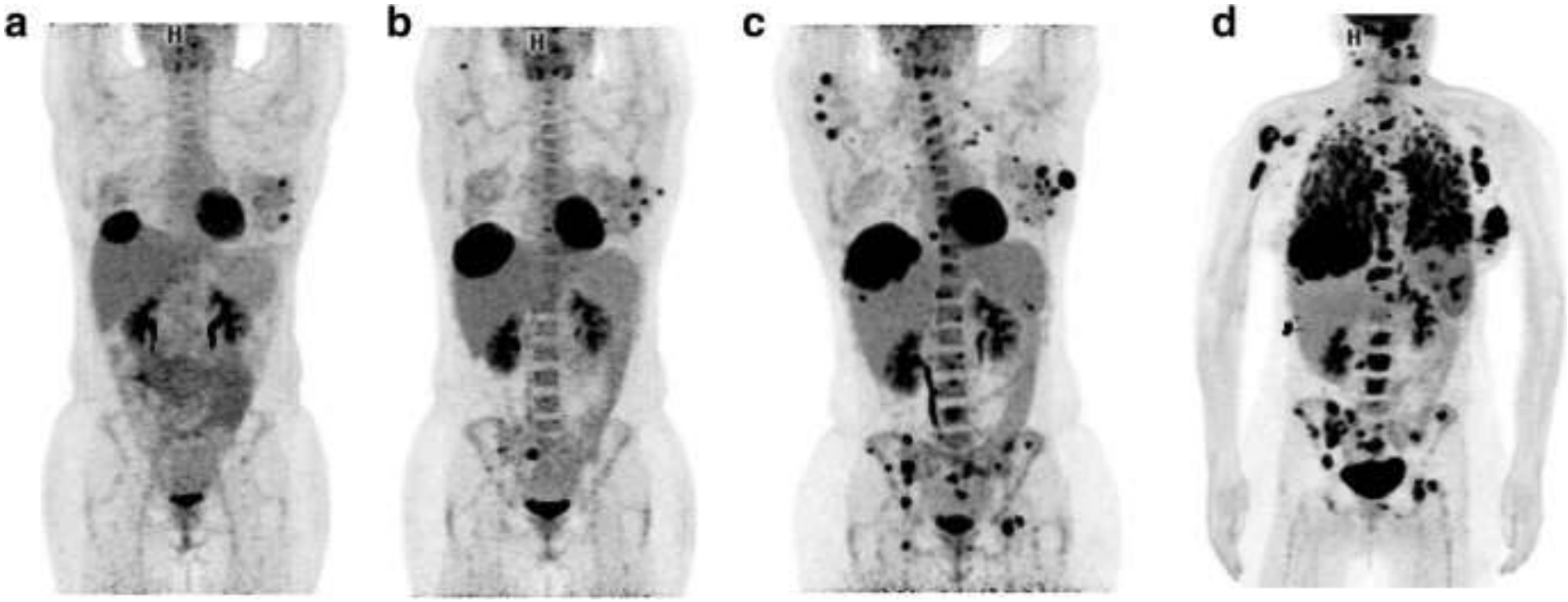
Tumor Volume Delineation



Tumor Volume Delineation

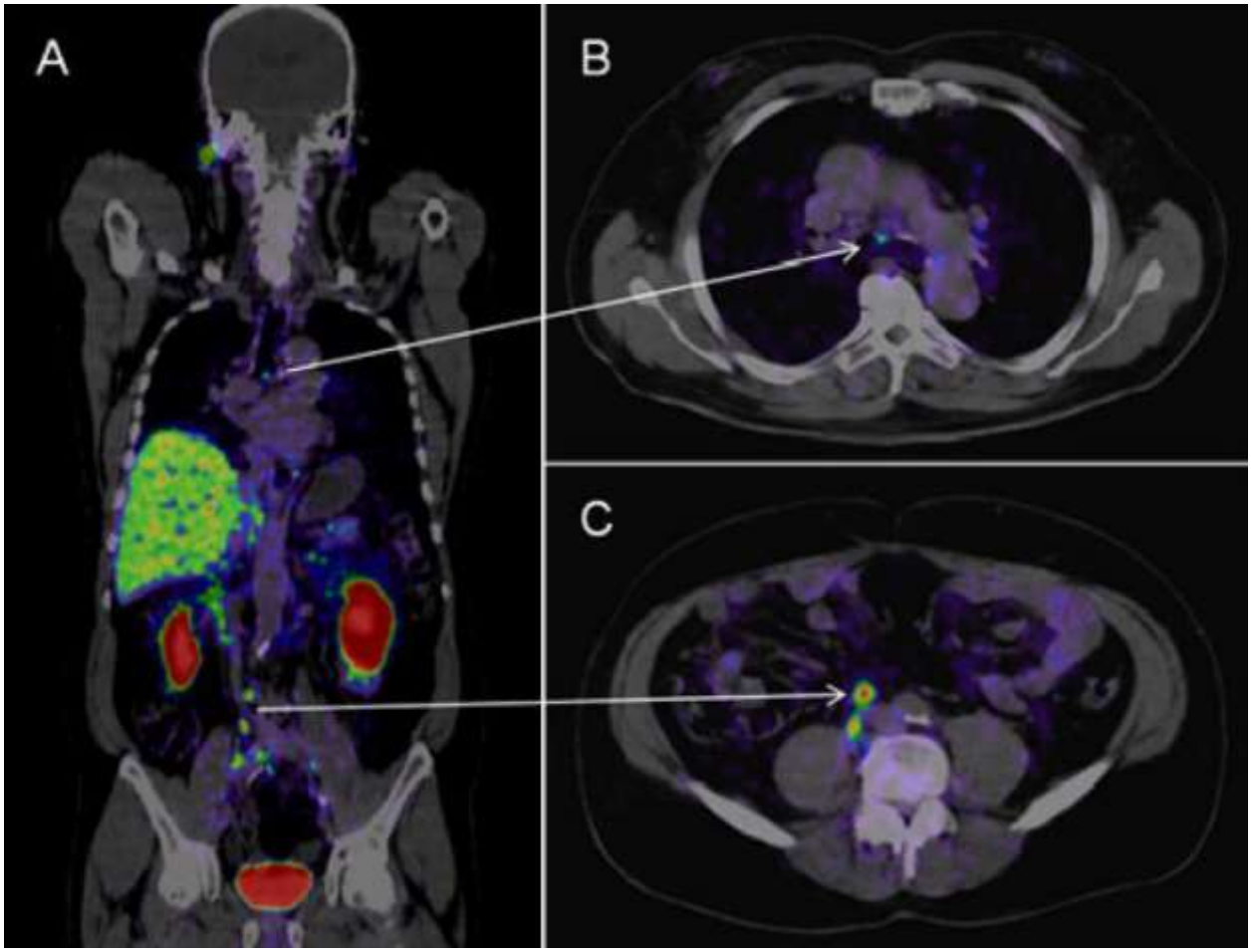


Disease Progression



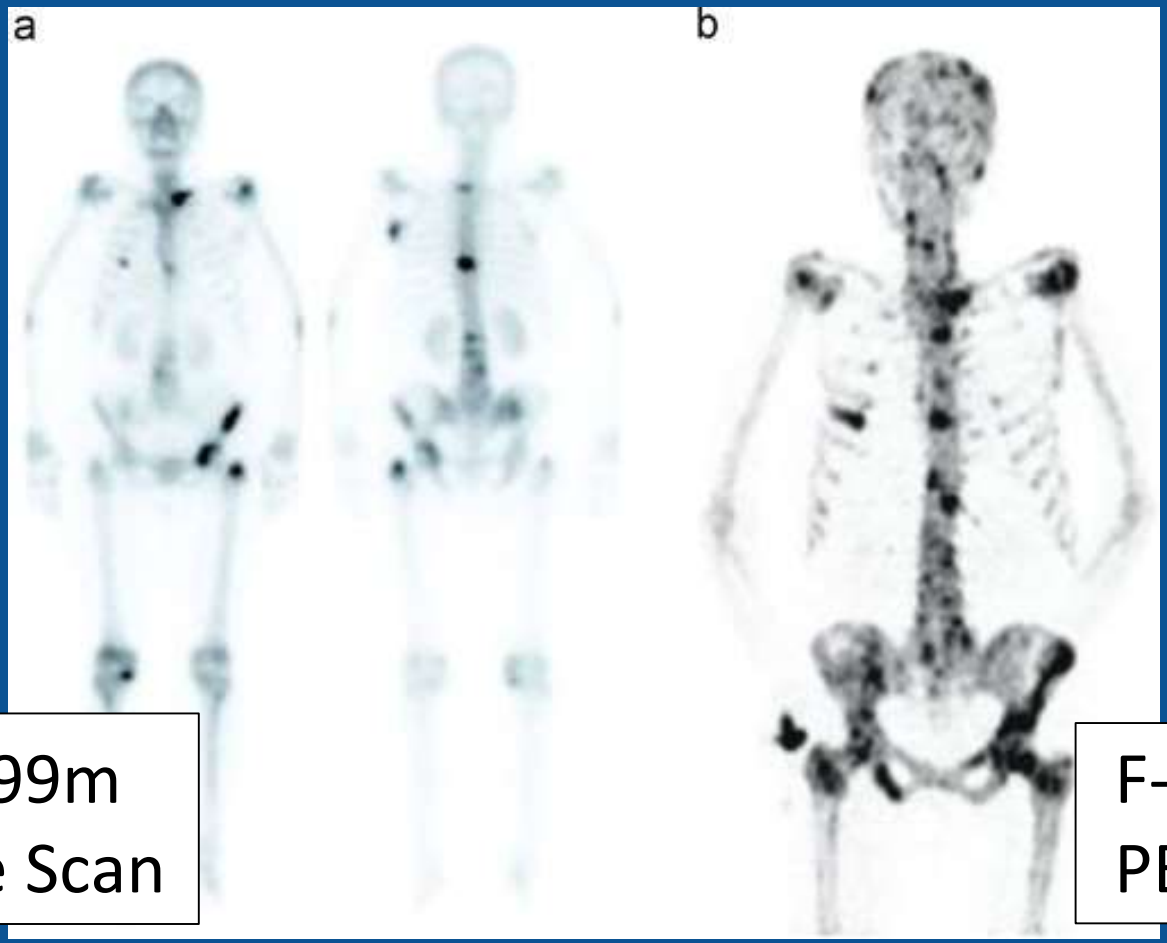
F-18 FDG-PET melanoma progression

Different Tracers



Ga - 68 PSMA PET-CT

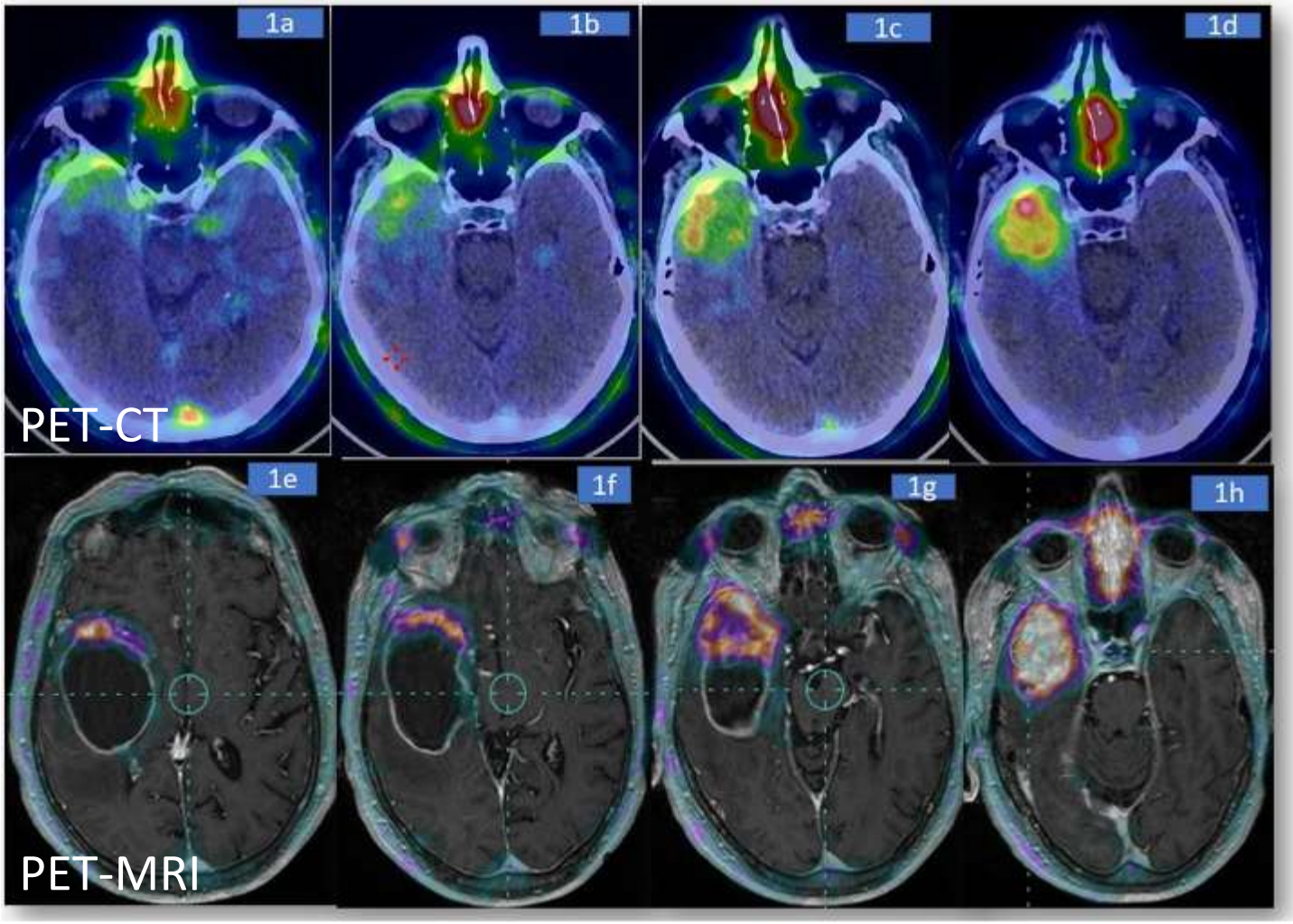
Different Tracers



Tc-99m Bone Scan

F-18 NaF PET Scan

Different Tracers

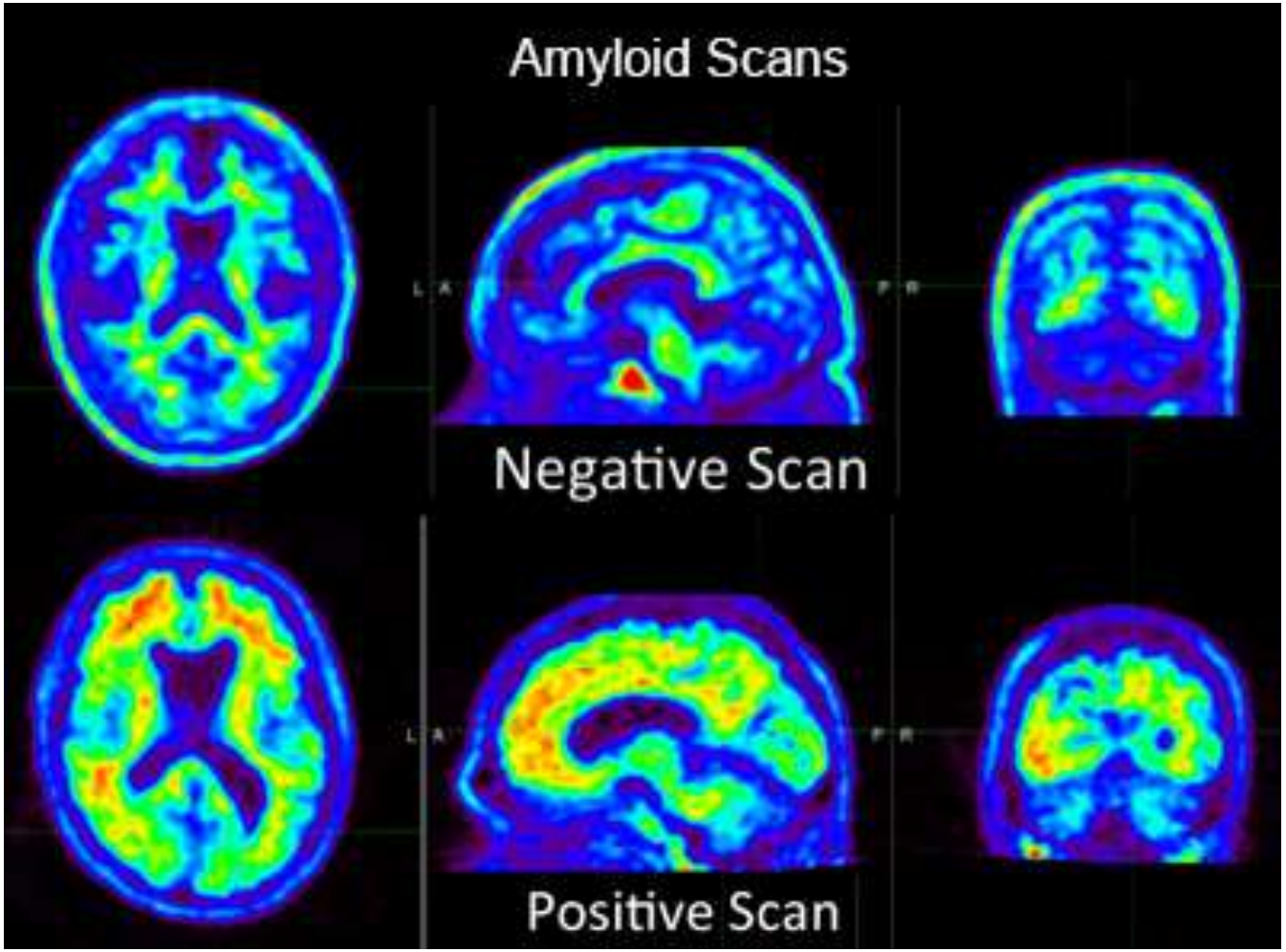


Cu-64 (ATSM)

Hypoxia targeting PET Tracer

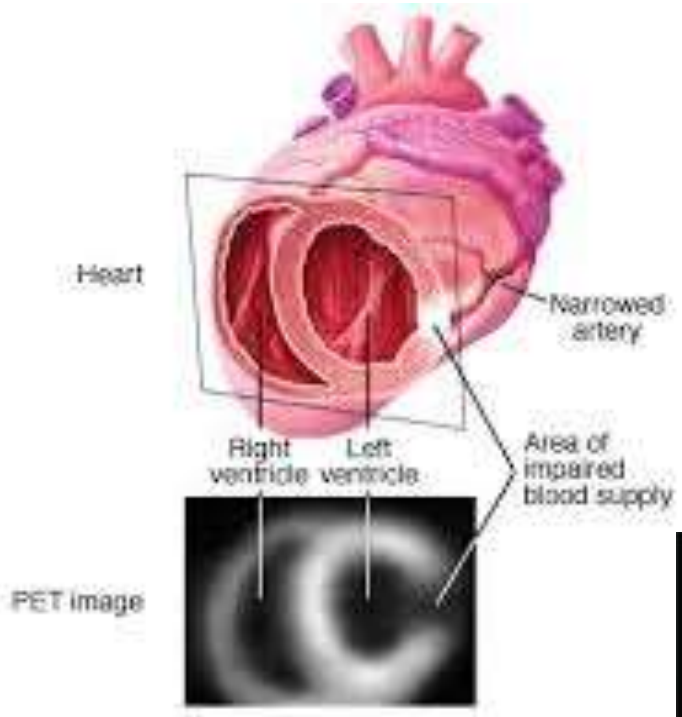
PET Applications
Neurology

Neurology – Alzheimer's

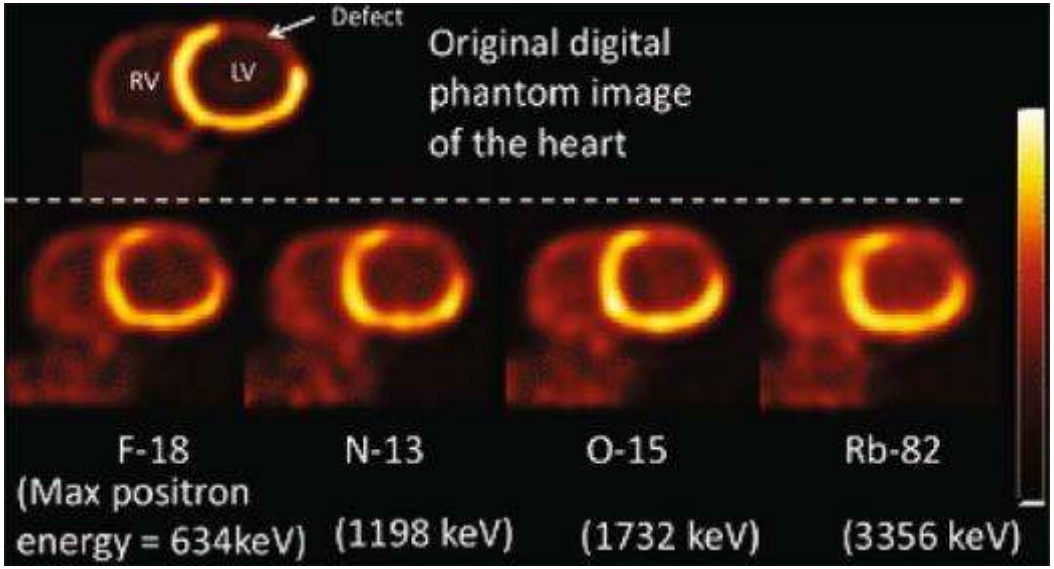


PET Applications
Cardiology

Cardiac PET



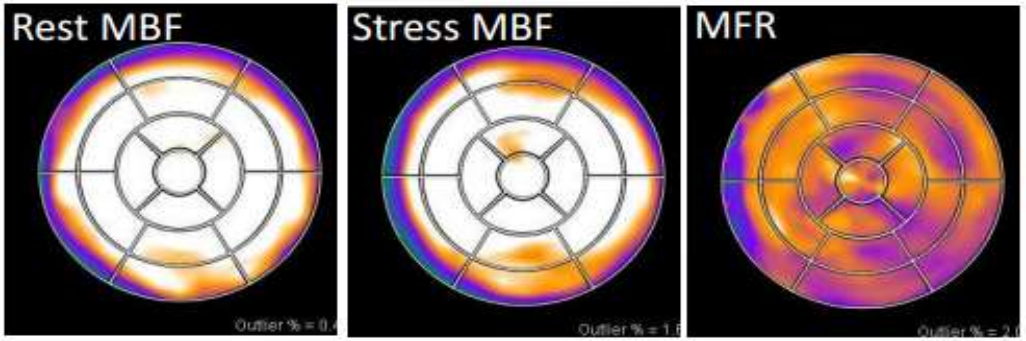
Cardiac PET gold standard for the non-invasive assessment of coronary artery disease



Blurring effect by positron range increases with higher positron kinetic energy

True Myocardial Blood Flow

Hull University Teaching Hospitals NHS Trust

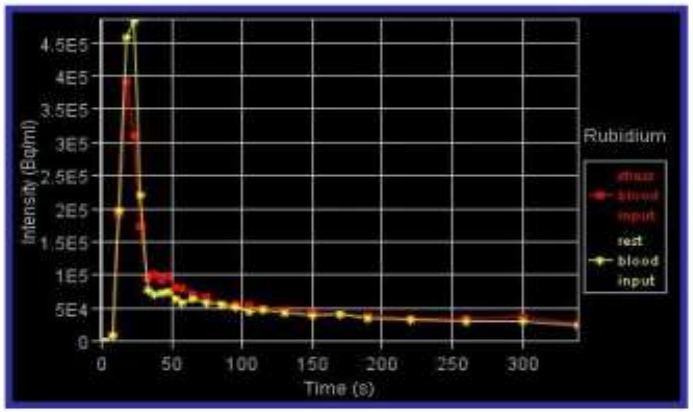


Myocardial Flow Reserve
=
Stress MBF / Rest MBF

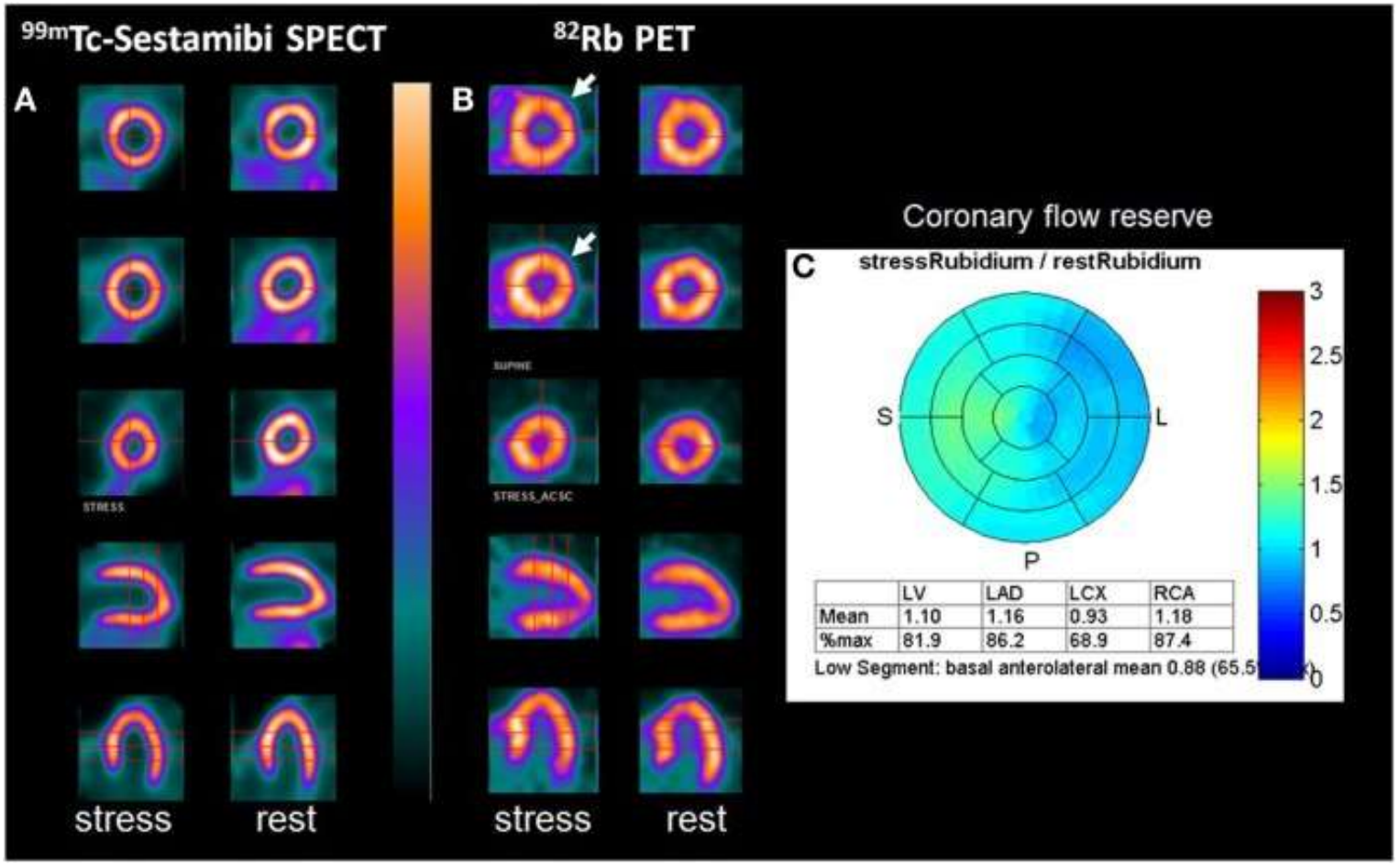
Normal Ranges
Rest MBF: 0.6 – 1.3 ml/gm/min
Stress MBF: 1.2 – 3.3 ml/gm/min

"Normal" MFR: > 2.0
"Equivocal" MFR: 1.5 – 2.0
"Abnormal" MFR: < 1.5

	QMP (ml/g/min)				Reserve	
	Stress		Rest			
	mean	std dev	mean	std dev	mean	std dev
LAD	2.47	0.61	0.93	0.17	2.67	0.63
LCX	2.42	0.58	0.90	0.23	2.72	0.33
RCA	2.81	0.70	0.93	0.26	3.10	0.54
Global	2.53	0.64	0.92	0.21	2.79	0.57



PET Myocardial Perfusion



Driessen RS *et al.* Myocardial Perfusion Imaging with PET. Int J Cardiovasc Imaging. 2017; 33(7): 1021-1031


Thank you for listening