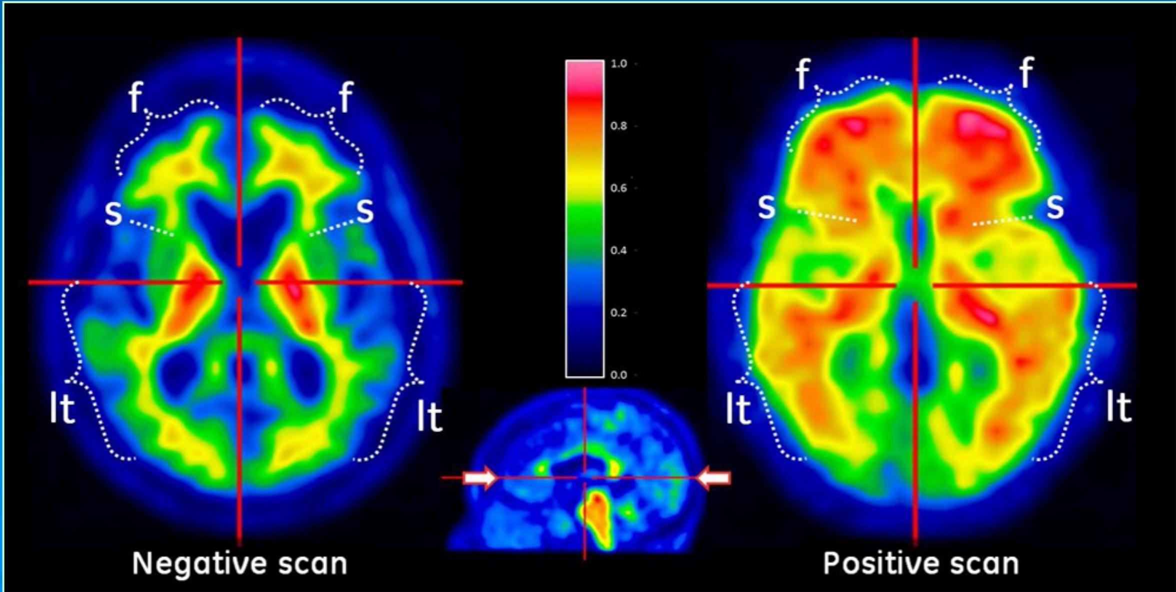
Nuclear Medicine SPECT & PET

Physics and instrumentation
Brain functional imaging

Nuclear Medicine

- Nuclear medicine is a branch of medical imaging that uses radionuclides for diagnosis and treatment of disease
- Radionuclides are combined with other chemical compounds to form radiopharmaceuticals

Beta Amyloid Imaging

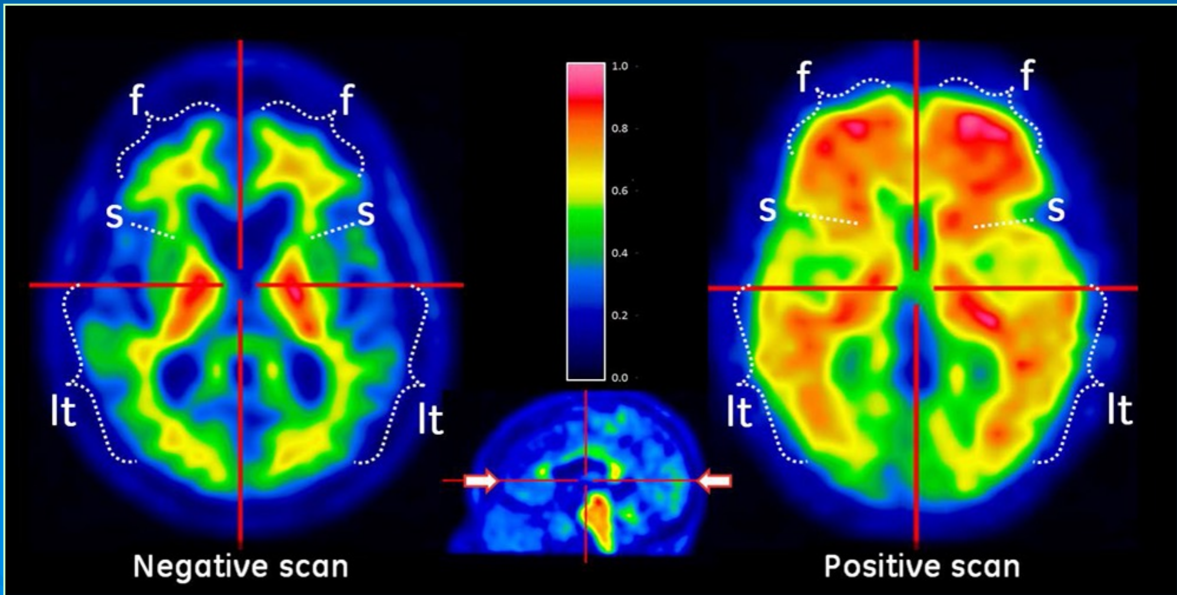


Nuclear Medicine

The radiopharmaceuticals

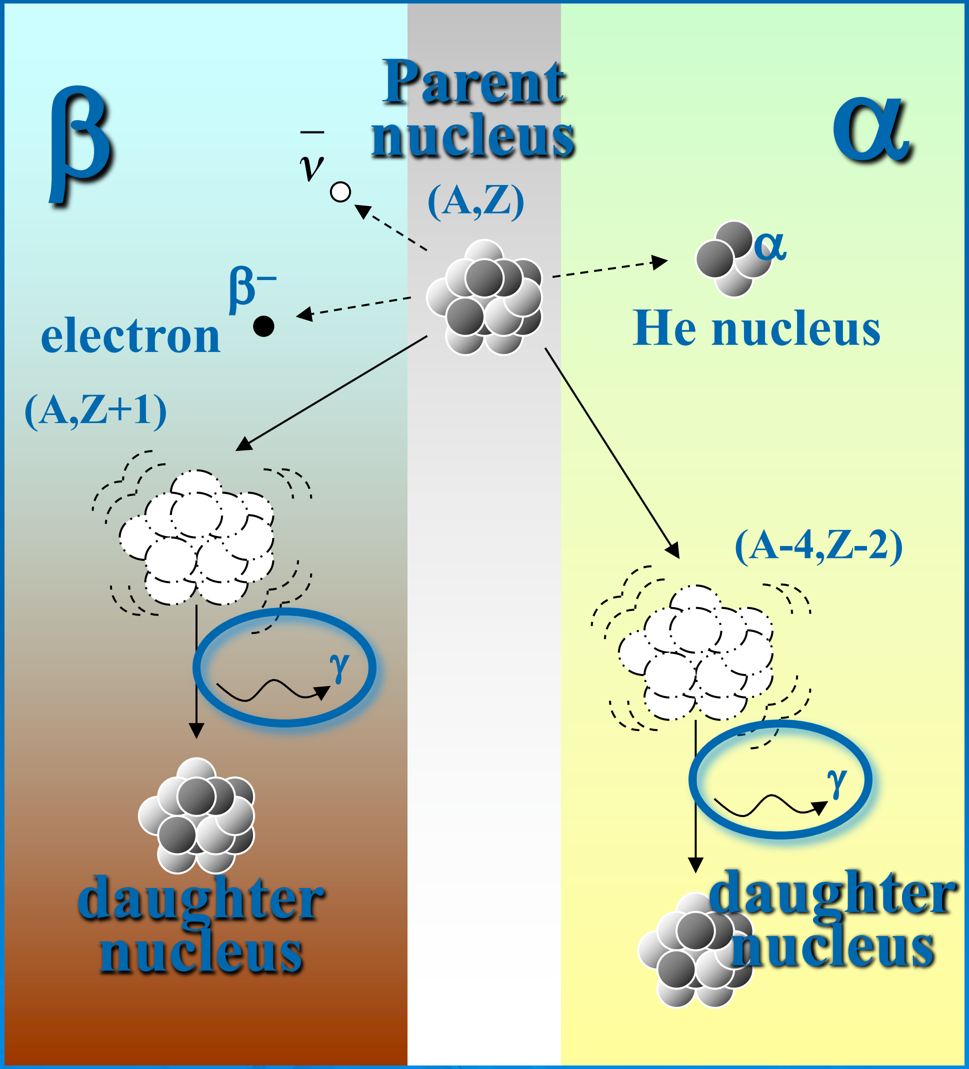
- localize to specific organs or cellular receptors
- allow to diagnose or treat a disease based on the cellular function and physiology
  - rather than relying on the anatomy

Beta Amyloid Imaging



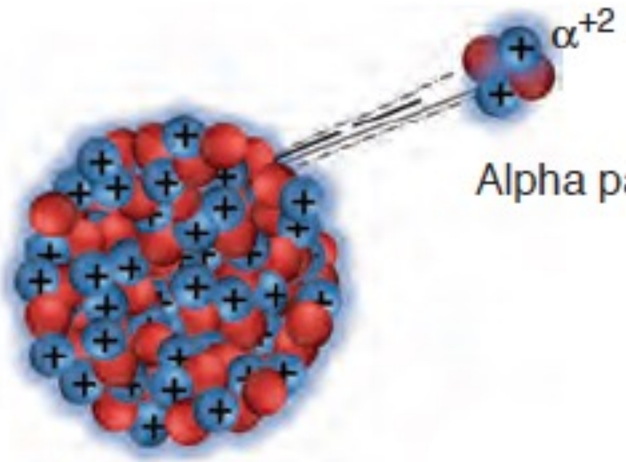
Radioactive nuclei

- The nucleus is consisting of protons (Z) and neutrons
  - A=protons (Z) + neutrons
- Radioactive isotopes have instable nuclei
  - If Z>83 the nucleus is radioactive
- In radioactive decays α or β rays are emitted
- **In both cases a γ ray is emitted**



Alpha decay

$$^{A}_{Z}X \rightarrow \, ^{A-4}_{Z-2}Y + \underset{\left(\substack{\text{alpha}\\\text{particle}}\right)}{^{4}_{2}He^{2+}} + \text{transition energy}$$



EXAMPLE:

$$^{220}_{86}Rn \rightarrow \, ^{216}_{84}Po + \, ^{4}_{2}He^{2+} + 6.4\text{ MeV transition energy}$$

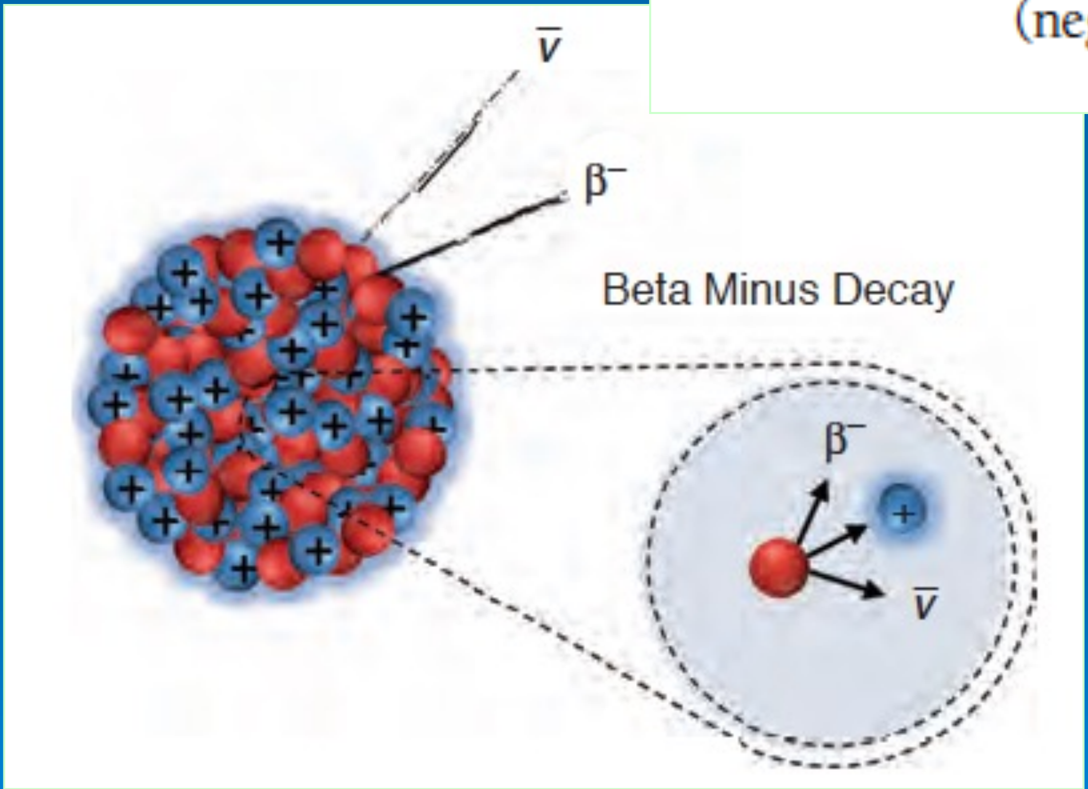
Alpha decay results in a large energy transition and a slight increase in the ratio of neutrons to protons (N/Z ratio):

$$^{220}_{86}Rn \xrightarrow{\alpha^{+2}} \, ^{216}_{84}Po$$

N/Z = 134/86 = 1.56   N/Z = 132/84 = 1.57

Beta-minus decay

$$^{A}_{Z}X \rightarrow {}^{A}_{Z+1}Y + \underset{\text{(negatron)}}{\beta^-} + \underset{\text{(antineutrino)}}{\bar{\nu}} + \text{energy}$$



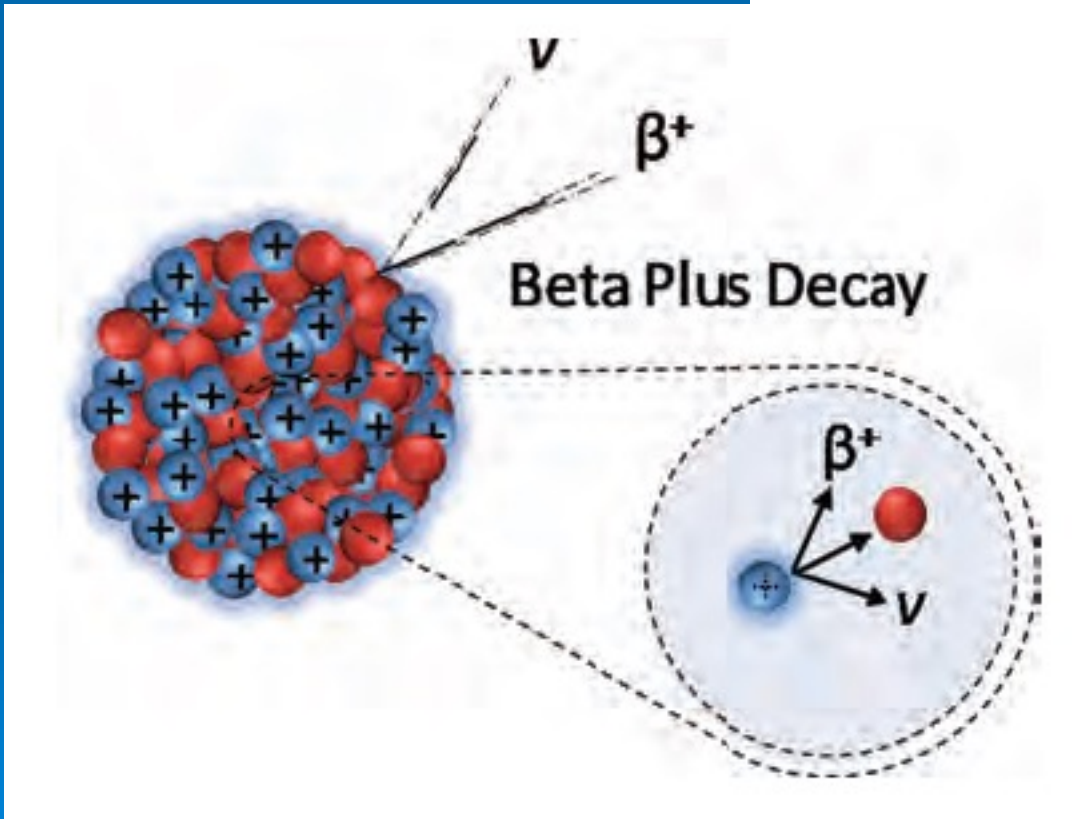
EXAMPLE:

$$^{32}_{15}P \xrightarrow{\beta^-} {}^{32}_{16}S$$

$N/Z = 17/15 = 1.13$ $\qquad$ $N/Z = 16/16 = 1.00$

Beta-plus decay

$${}^{A}_{Z}X \rightarrow {}^{A}_{Z-1}Y + \underset{(\text{positron})}{\beta^{+}} + \underset{(\text{neutrino})}{\nu} + \text{energy}$$



EXAMPLE:

$${}^{18}_{9}F \xrightarrow{\beta^{+}} {}^{18}_{8}O$$

$N/Z = 9/9 = 1$ $\qquad$ $N/Z = 10/8 = 1.25$

Radioactive decay

- N_0 initial number of radioactive atoms
- N_t number of radioactive atoms at time t
- A_0 initial activity
- λ decay constant
- Half-live: time required for the number of radioactive atoms in a sample to decrease by one-half

$$N_t = N_0 e^{-\lambda t} \text{ or } A_t = A_0 e^{-\lambda t}$$

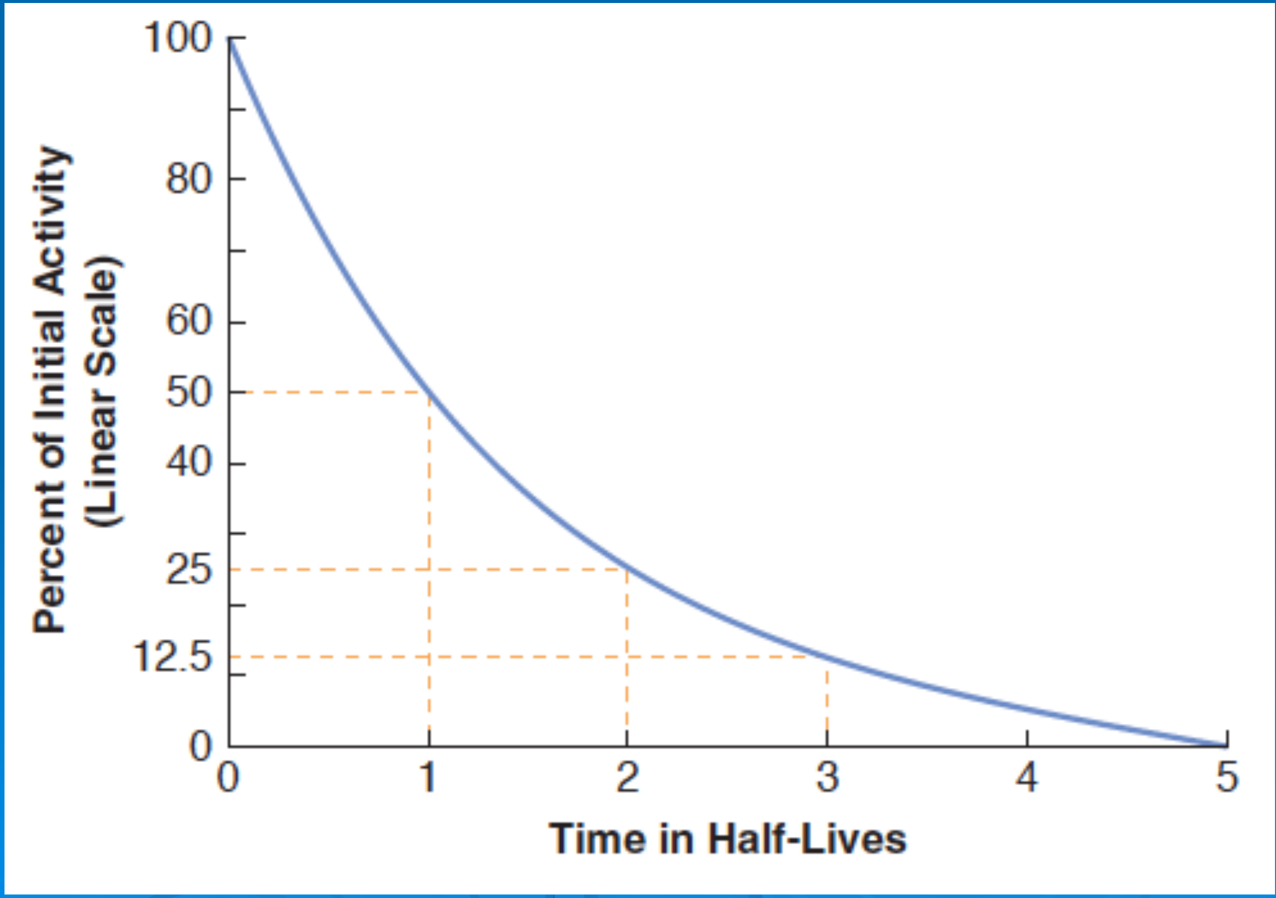


TABLE 15-1 UNITS AND PREFIXES ASSOCIATED WITH VARIOUS QUANTITIES OF RADIOACTIVITY

QUANTITY	SYMBOL	DPS	DPM
Gigabecquerel	GBq	1×10^9	6×10^{10}
Megabecquerel	MBq	1×10^6	6×10^7
Kilobecquerel	kBq	1×10^3	6×10^4
Curie	Ci	3.7×10^{10}	2.22×10^{12}
Millicurie	mCi (10^{-3} Ci)	3.7×10^7	2.22×10^9
Microcurie	μCi (10^{-6} Ci)	3.7×10^4	2.22×10^6
Nanocurie	nCi (10^{-9} Ci)	3.7×10^1	2.22×10^3
Picocurie	pCi (10^{-12} Ci)	3.7×10^{-2}	2.22

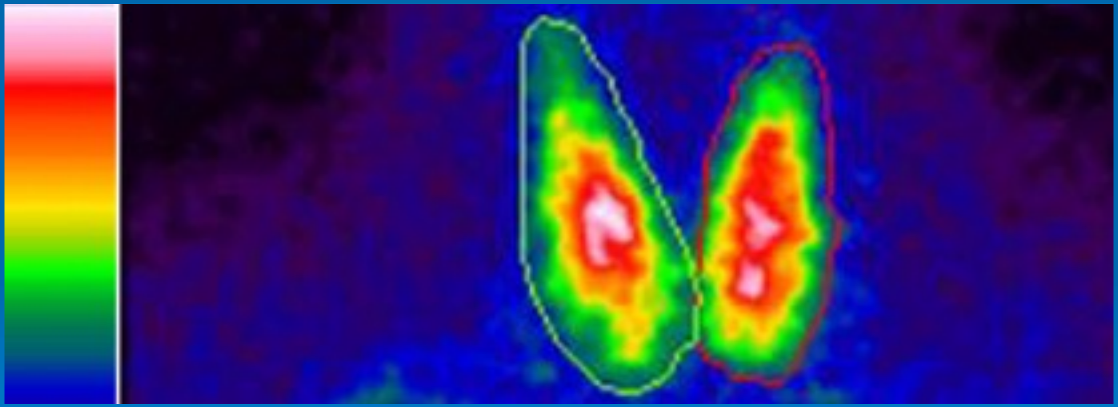
Multiply mCi by 37 to obtain MBq or divide MBq by 37 to obtain mCi (e.g., 1 mCi = 37 MBq).

DPS: decays per second
DPM decays per minute

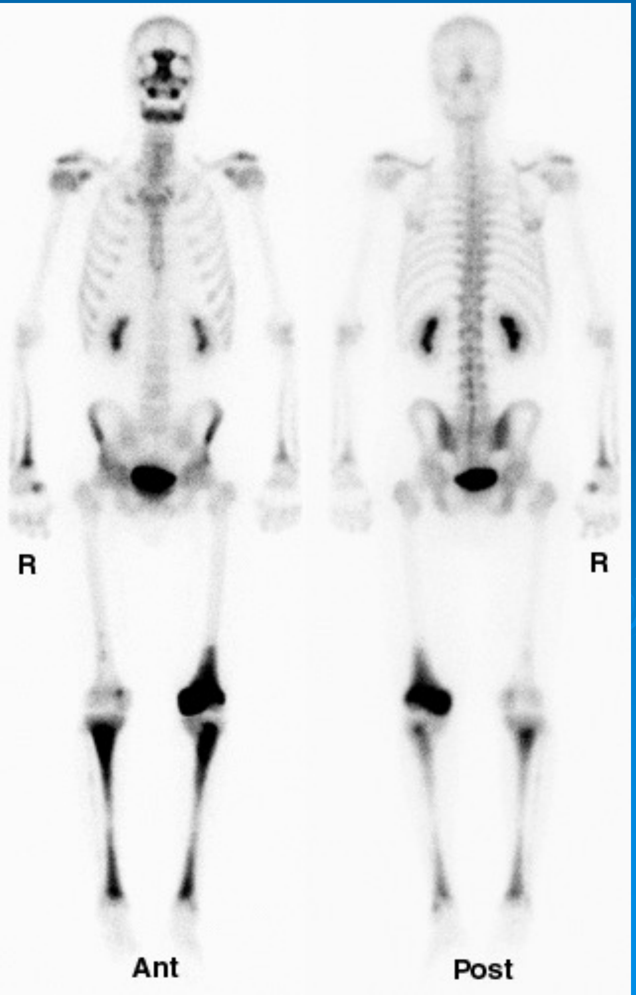
Curie: traditional units

Nuclear Medicine

The radiopharmaceuticals can localize to specific organs or cellular receptors



Thyroid scintigraphy



bone scintigraphy

Radionuclides for nuclear medicine

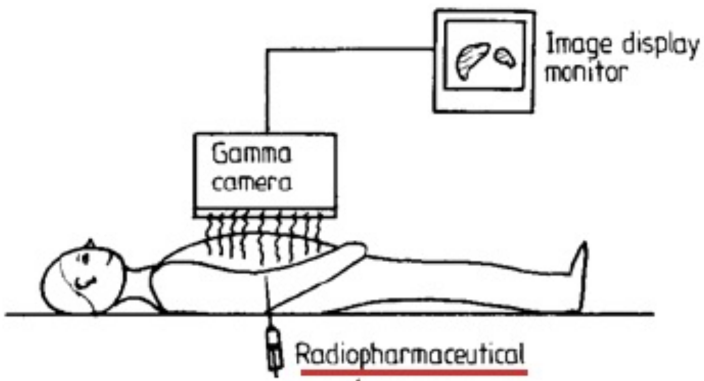
Radionuclides Commonly Used in Scintigraphy and SPECT

Radionuclide	Half-life	Energies of Primary Photons (keV)
Technetium-99m	6 h	140
Thallium-201	73 h	~72
Gallium-67	3.3 d	88, 185, 300
Iodine-131	8.04 d	365
Iodine-123	13.2 h	159
Xenon-127	36.4 d	172, 203, 375
Xenon-133	5.25 d	81, 161

- Nuclear medicine images are obtained with γ emission (photons) only
- Half-time: time required for the number of radioactive atoms in a sample to decrease by one-half

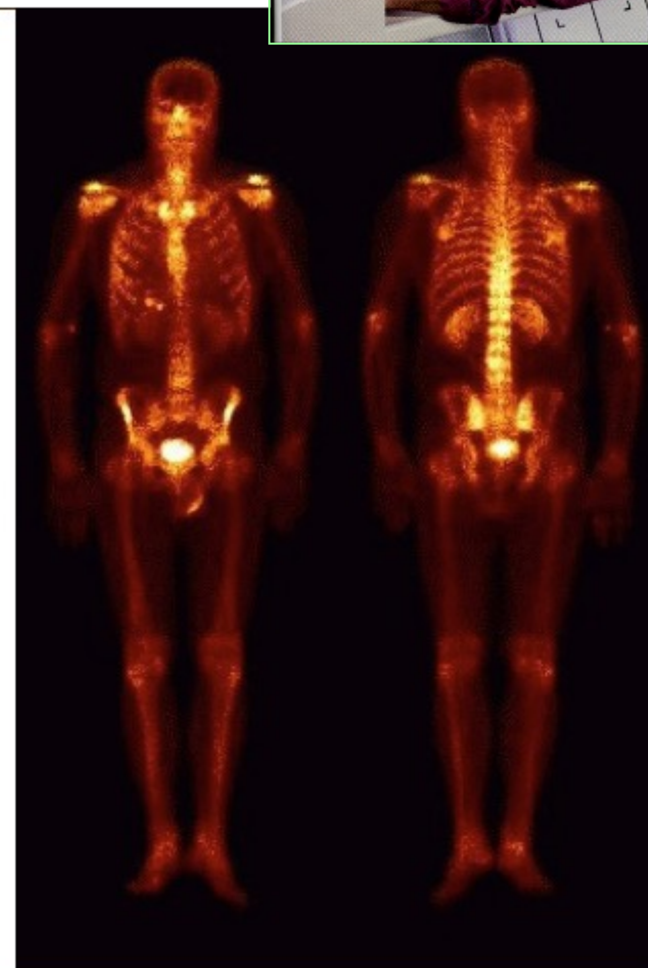
Scintigraphy

Nuclear Imaging with a Gamma Camera

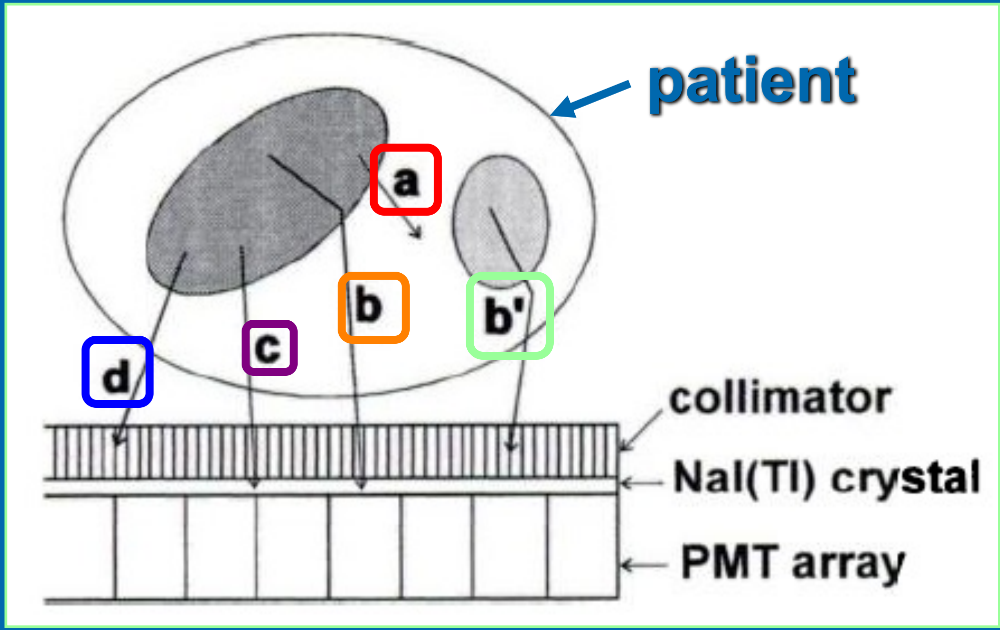


Radioactive atom held within a pharmaceutical molecule, allowing specific localization and imaging

Often used to search for bone metastases of cancer tumors



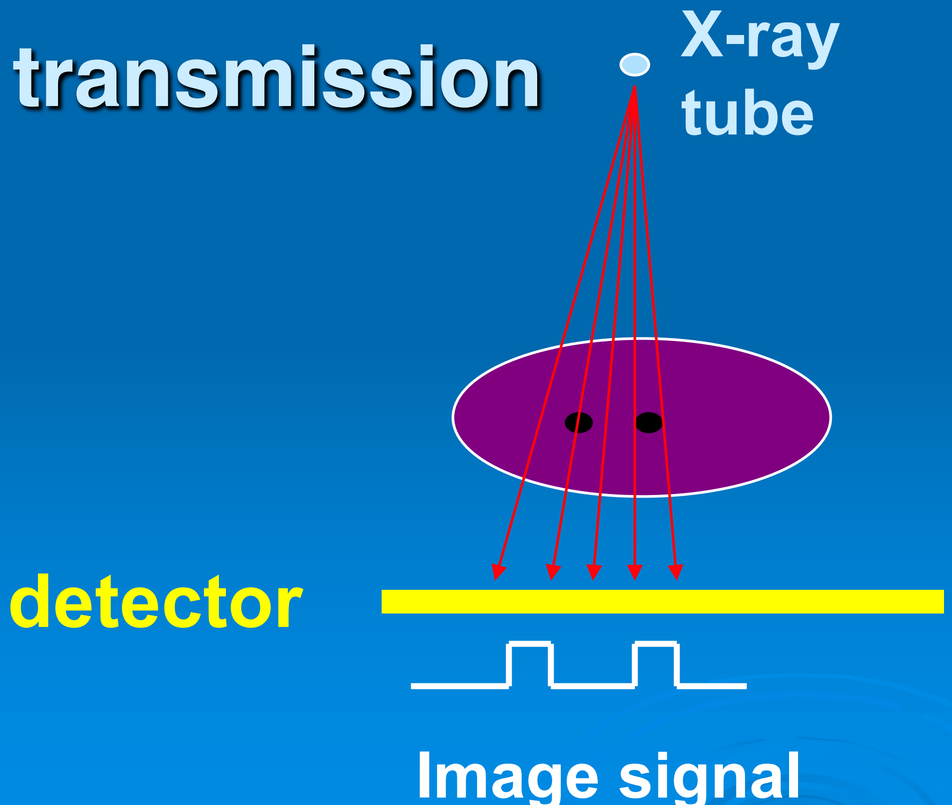
Gamma camera



- Diagram of photon interactions inside a patient and collimation of the exiting photons before detection
  - a indicates interaction in which the photon is totally absorbed by an atom
  - b and b' indicate a scatter interaction in which the photon changes its direction of travel
  - B and c pass through holes of the collimator and are detected by the detector
  - b' and d are photons that are blocked by the collimator hole septa and are not detected by the detector

Image acquisition

Difference between radiology (transmission) and nuclear medicine (emission)



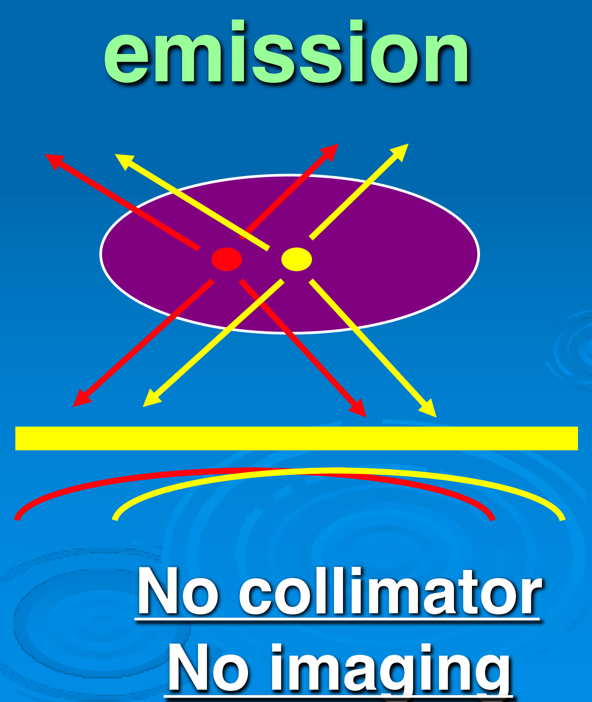
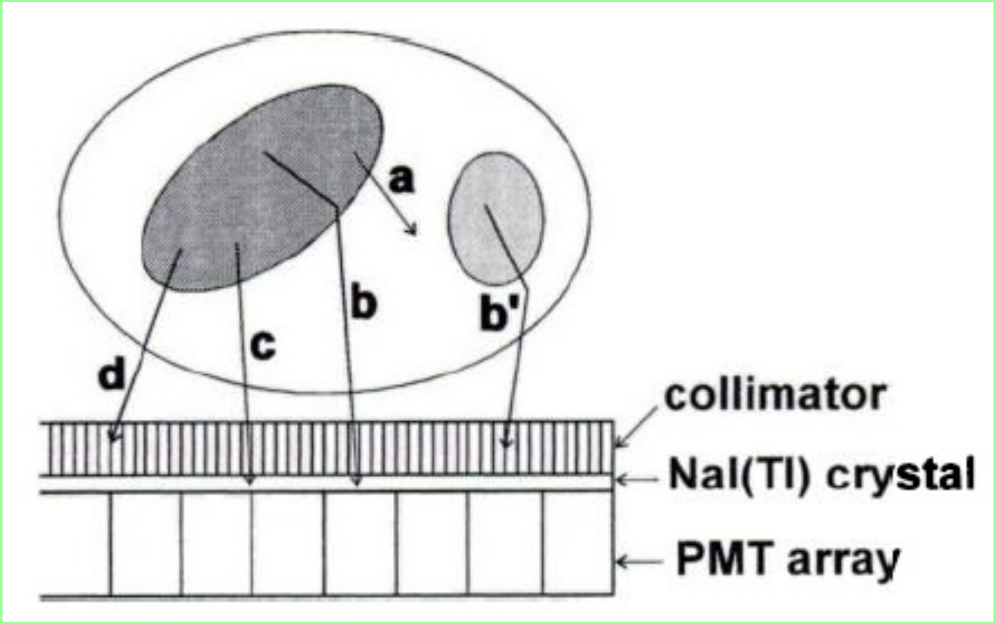
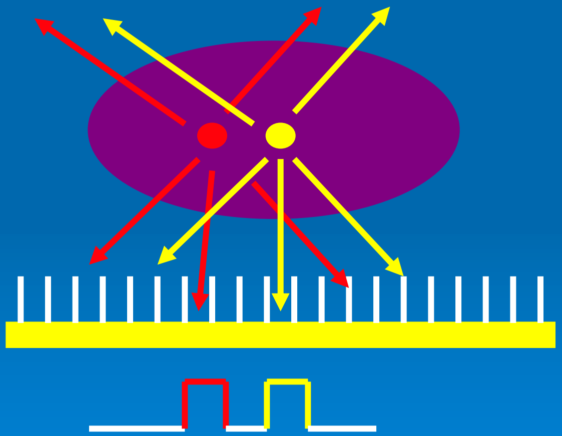


Image acquisition
Scintigraphy

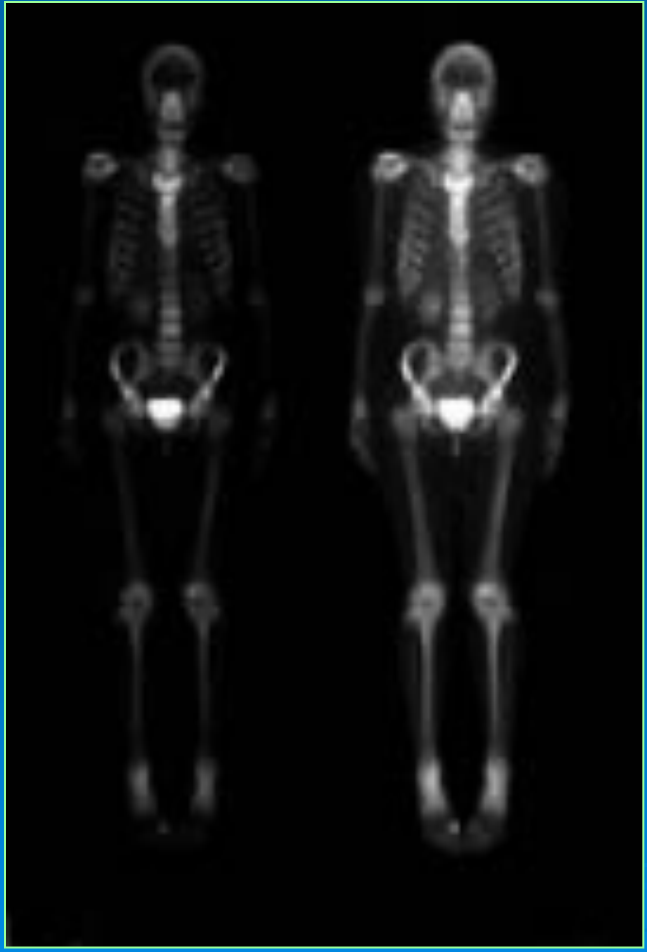


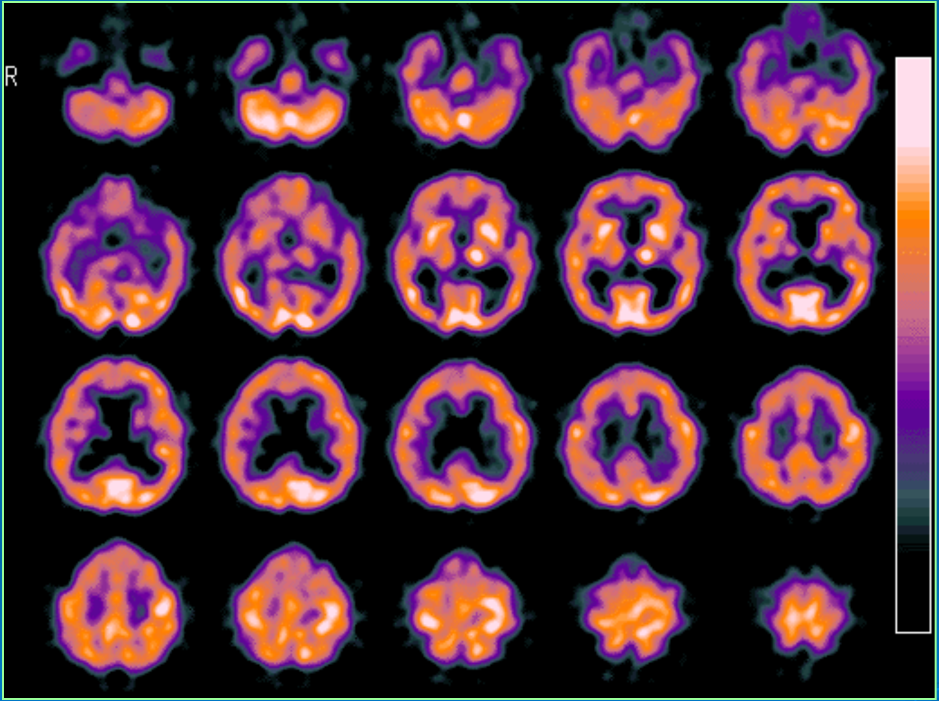
emission



With collimator

From planar imaging to tomography (SPECT)

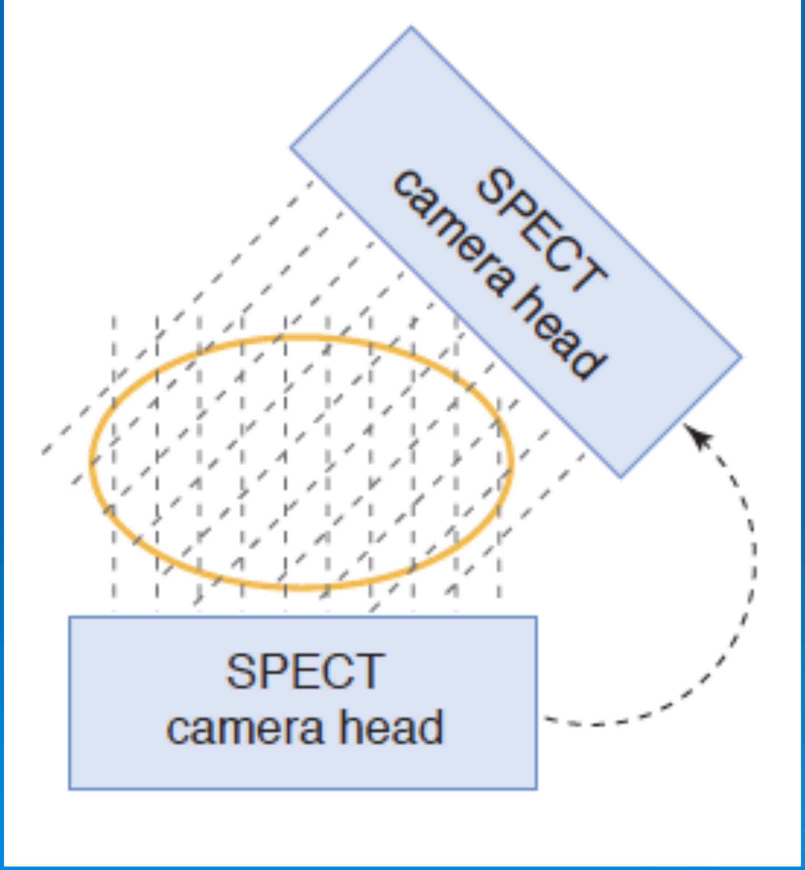


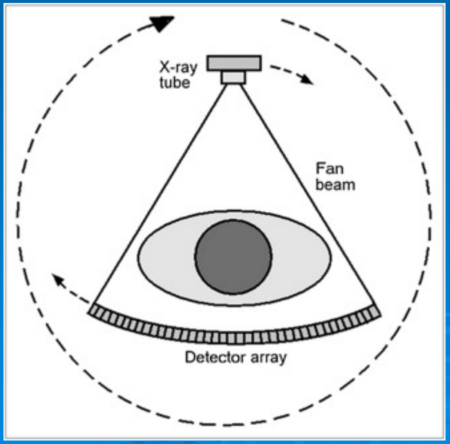


- SPECT

Single Photon Emission Computed Tomography

SPECT set-up

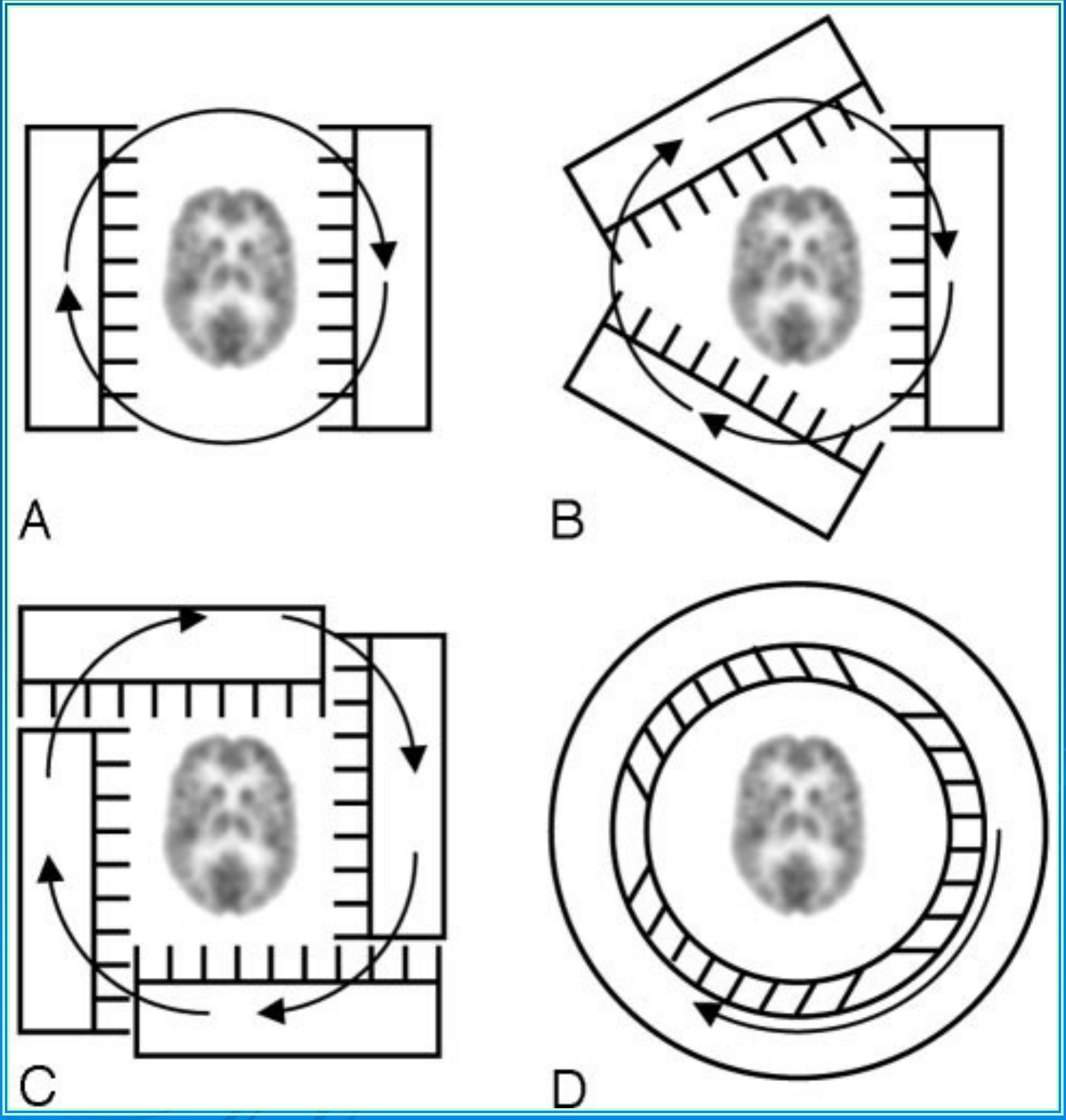




CT scanner

SPECT image acquisition

To allow tomographic reconstruction multiple images are necessary in different detector position around the patient



SPECT imaging in cerebrovascular disease

- Measurement of regional cerebral blood flow (rCBF)
- Sensitive indicator of perfusion
- Diagnosis and prognosis of cerebro-vascular disease

SPECT perfusion image

- Acute brain ischemia
- Perfusion defects after resolution of TIA
- Cerebral infarction
- Delayed ischemic deficits after SAH
- Determine pathophysiological mechanisms of stroke
- Monitor medical and surgical therapies

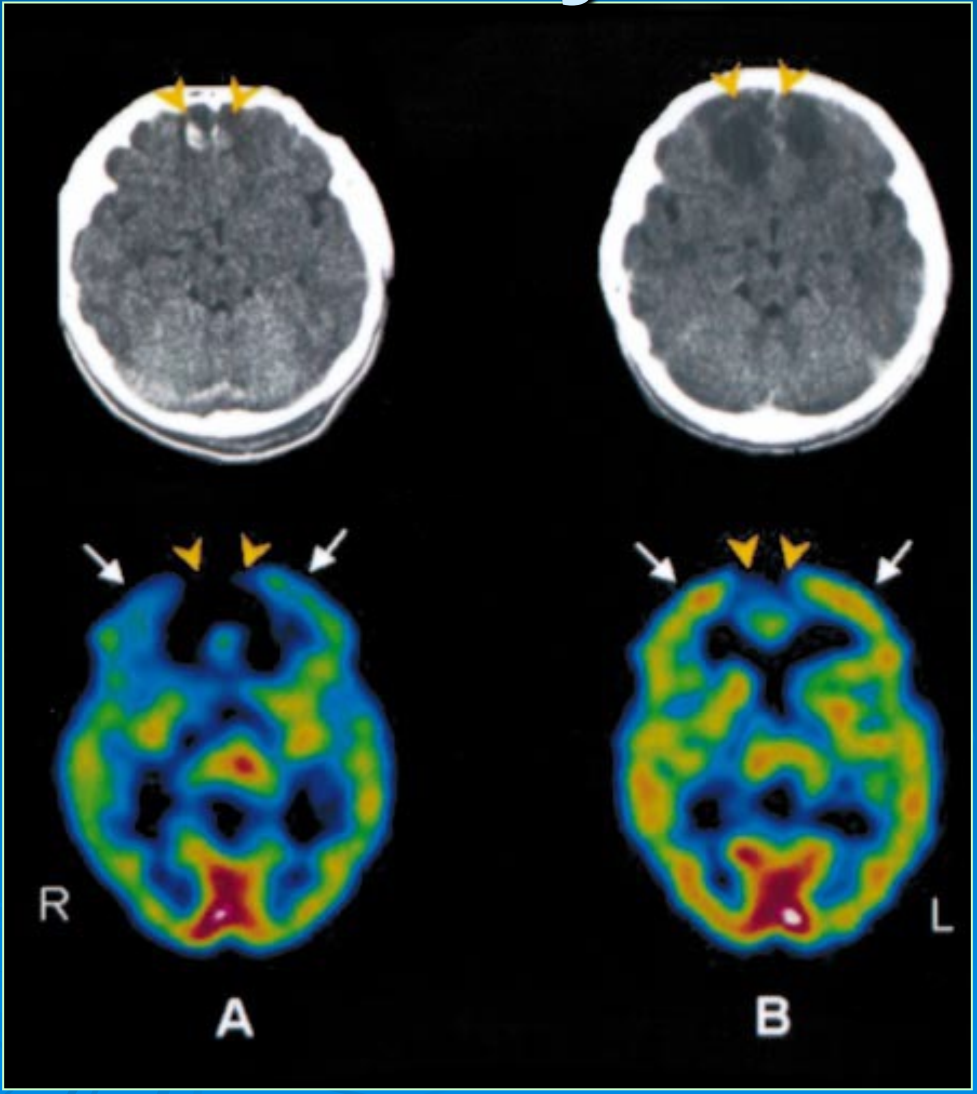
Perfusion study

CT and 99mTc SPECT images from 16-y-old patient with traumatic brain injury

(A) at time of admission shows subarachnoid hemorrhage with small contusional hemorrhagic foci in both frontal lobes (orange arrow)

(B) images obtained 1 mo later at time of discharge after clinical recovery

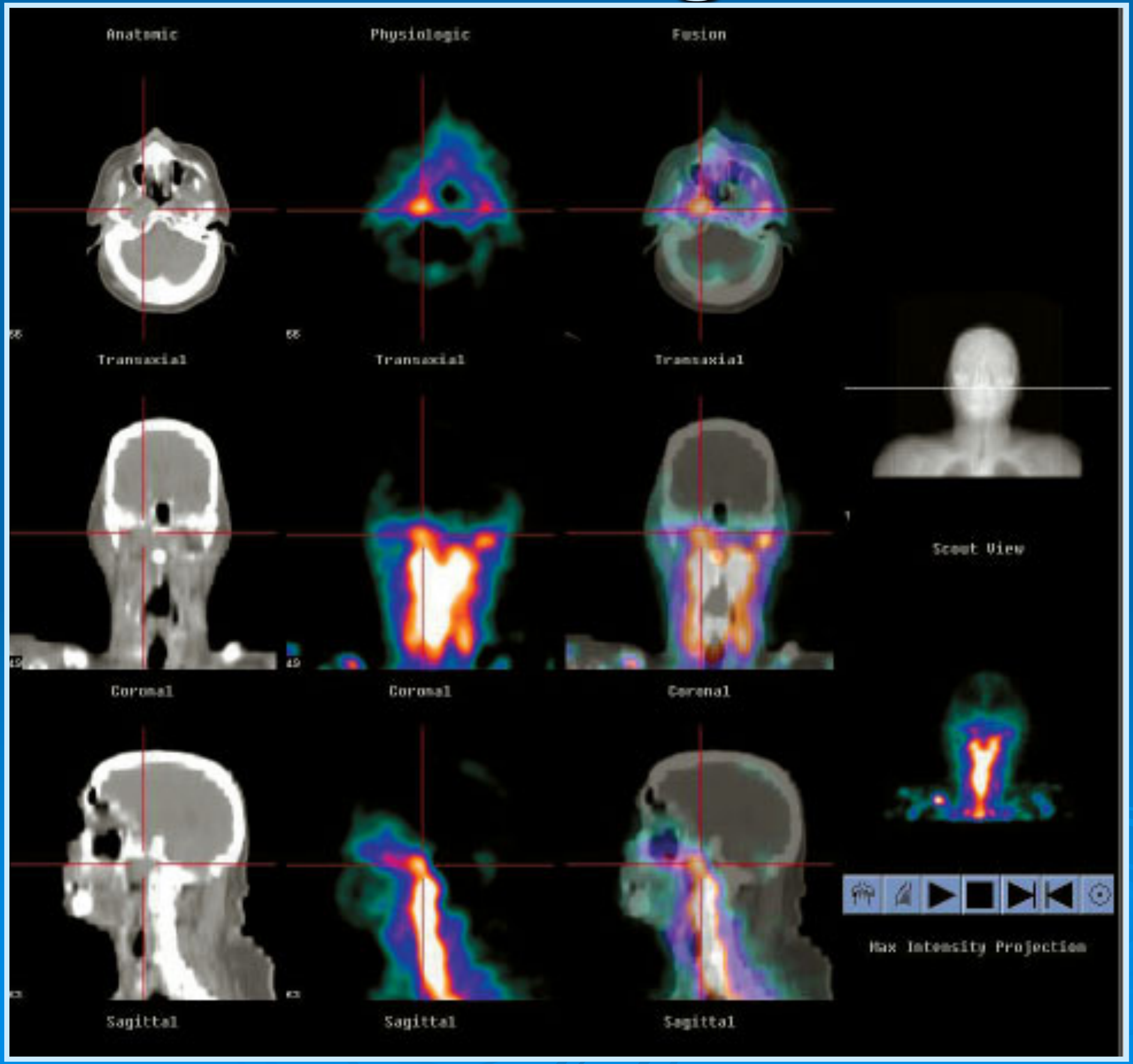
- Hypodense images in both frontal lobes can be seen on CT as consequence of hematoma's resolution
- Corresponding cold areas persist on SPECT image (orange arrow) but show improvement in global cerebral perfusion, particularly in both frontal lobes (white arrows)



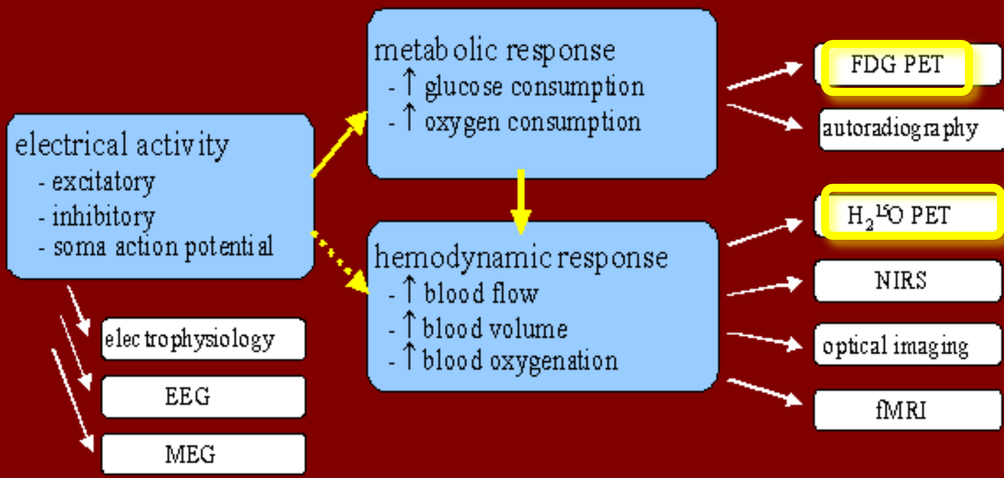
SPECT/CT scanner

A

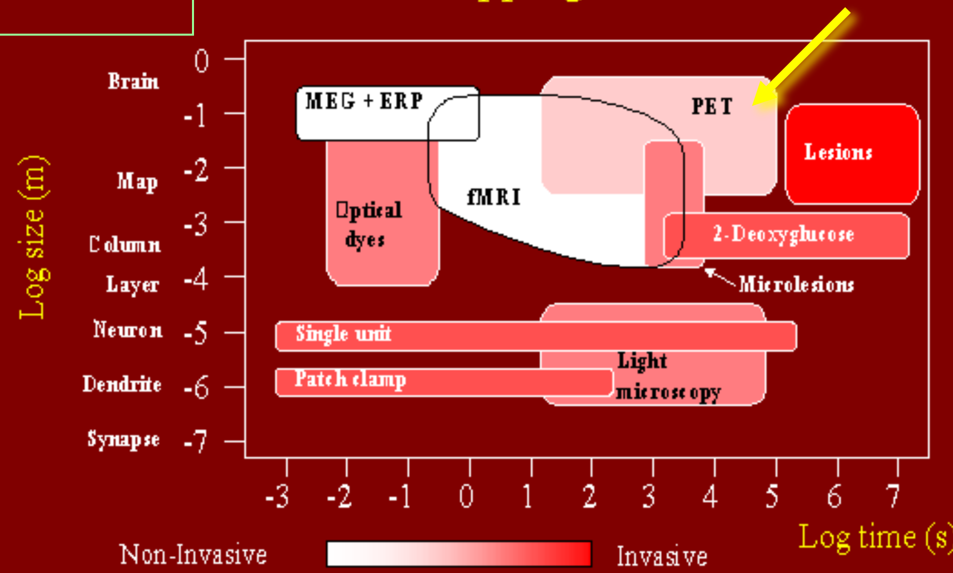
SPECT/CT Image fusion



Physiological Correlates of Brain Electrical Activity

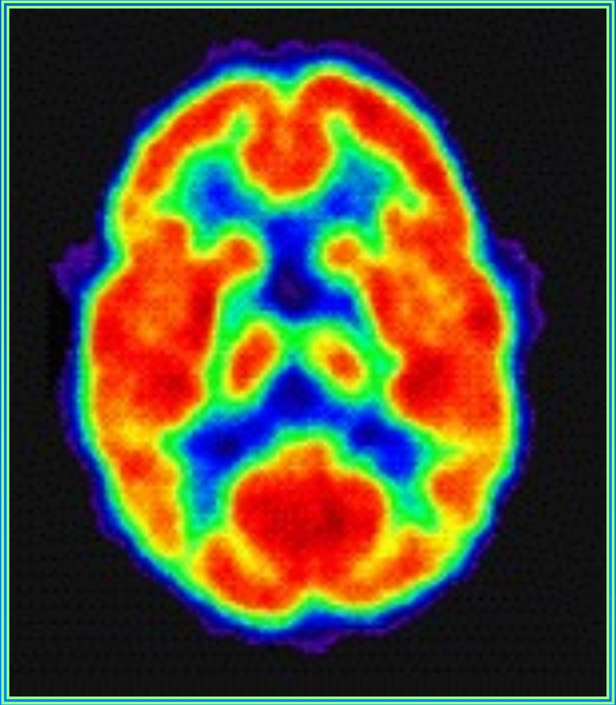


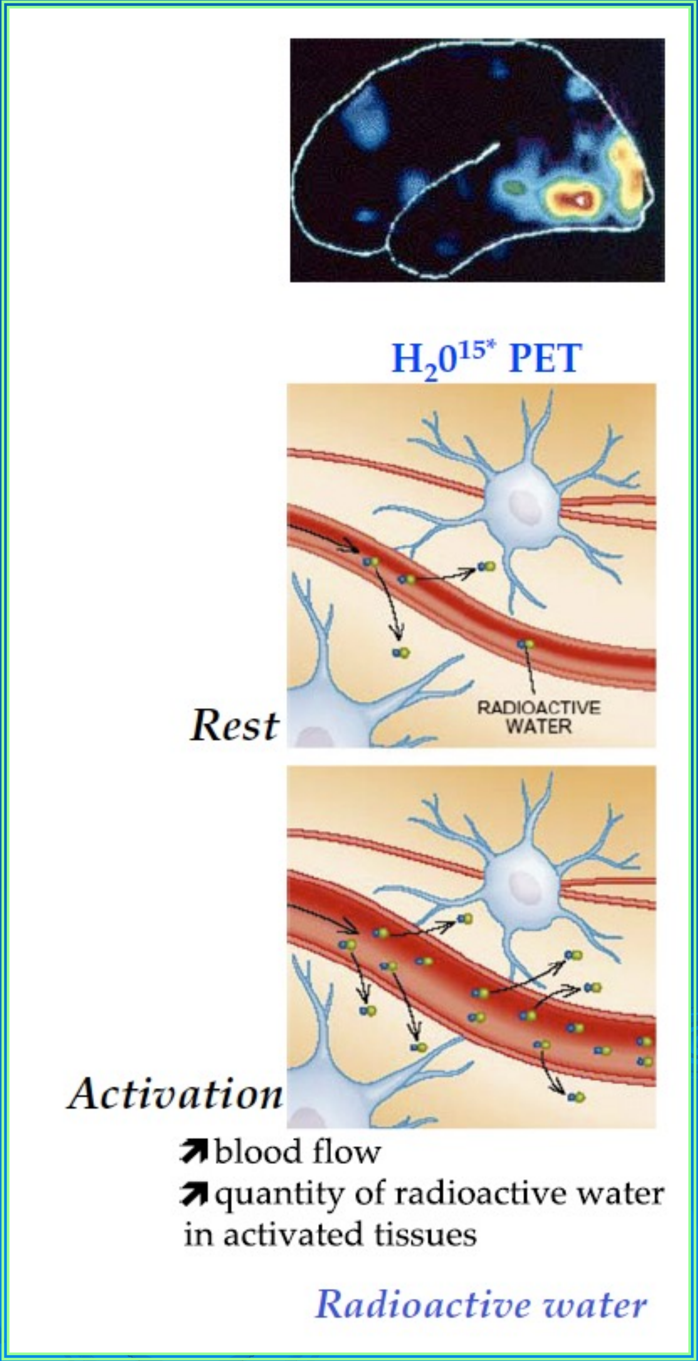
Functional Mapping Methods



PET images

- Blood flow studies
  - $H_2{}^{15}O$
- Metabolic activity
  - FDG





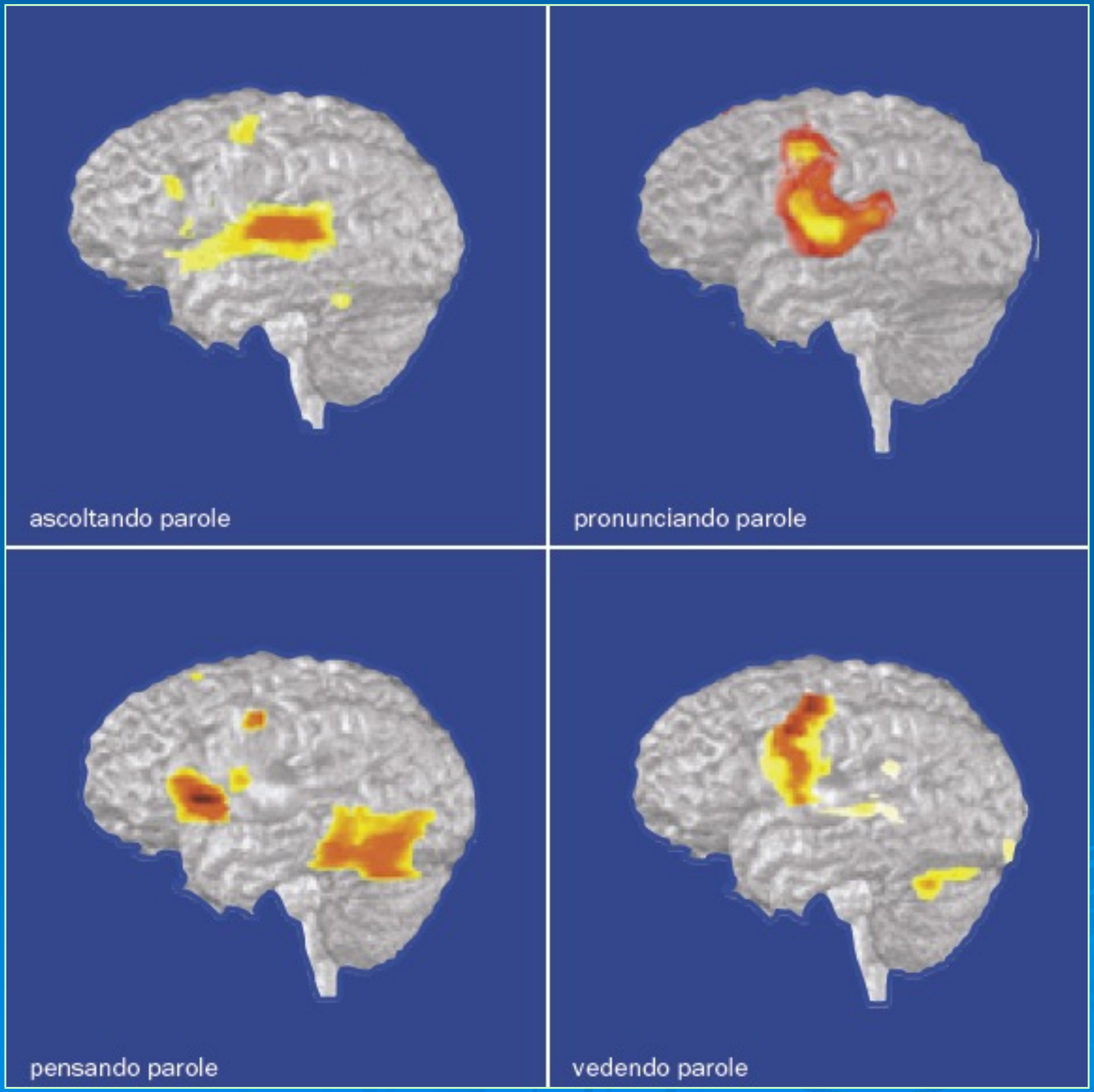
D. Le Bihan Phys. Med. Biol. 52 (2007) R57–R90

PET brain mapping

The first PET studies involving activation brain imaging emerged in the 1980s

- intravenously administered ^{15}O-water for measurement of regional cerebral blood flow
  - rCBF
- a sensitive method for quantifying regional brain activation during specific tasks

PET brain mapping



Positron is antimatter

What is a Positron?

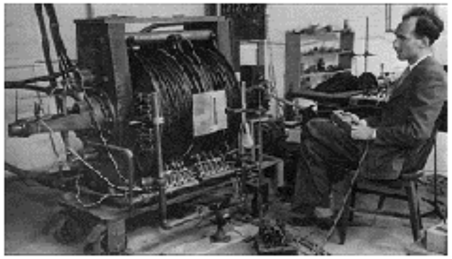
antiparticle to the electron

same mass: 9.11×10^{-31} kg (511 keV)

opposite charge: $+1.6 \times 10^{-19}$ C

lifetime very short because free positrons rapidly combine with an electron

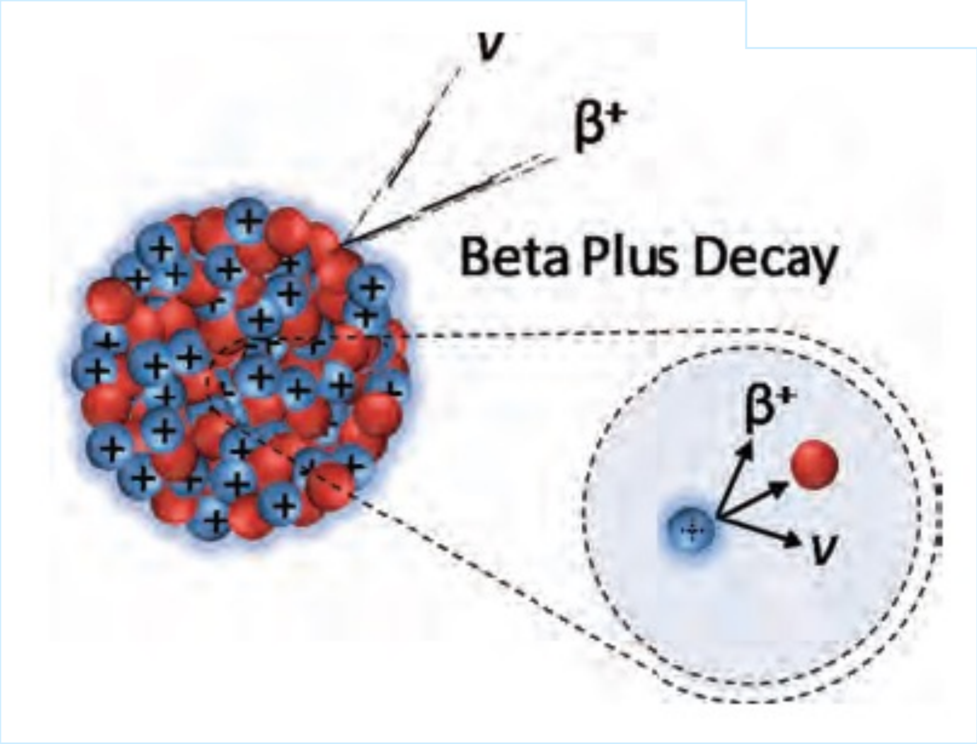
Discovery of the Positron (Anderson, 1932)



Anderson was using a cloud chamber containing a thin lead plate to investigate cosmic radiation. The experimental apparatus was placed in a magnetic field to allow the mass and charge of particles in the cloud chamber to be determined.

Beta-plus decay

$$ {}^{A}_{Z}X \rightarrow {}^{A}_{Z-1}Y + \underset{\text{(positron)}}{\beta^{+}} + \underset{\text{(neutrino)}}{\nu} + \text{energy} $$



EXAMPLE:

$$ {}^{18}_{9}F \xrightarrow{\beta^{+}} {}^{18}_{8}O $$

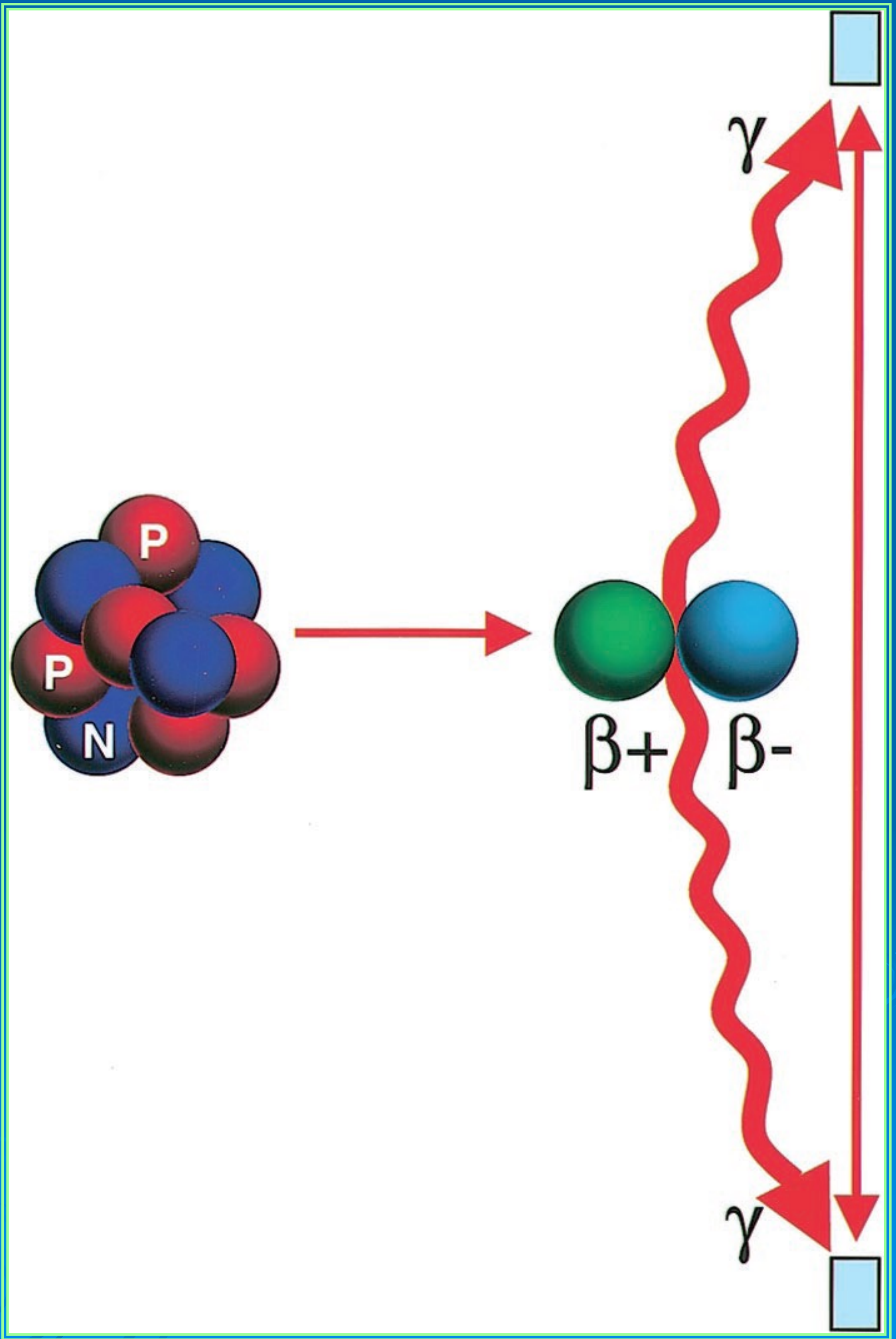
$N/Z = 9/9 = 1$ $\qquad$ $N/Z = 10/8 = 1.25$

Annihilation reaction

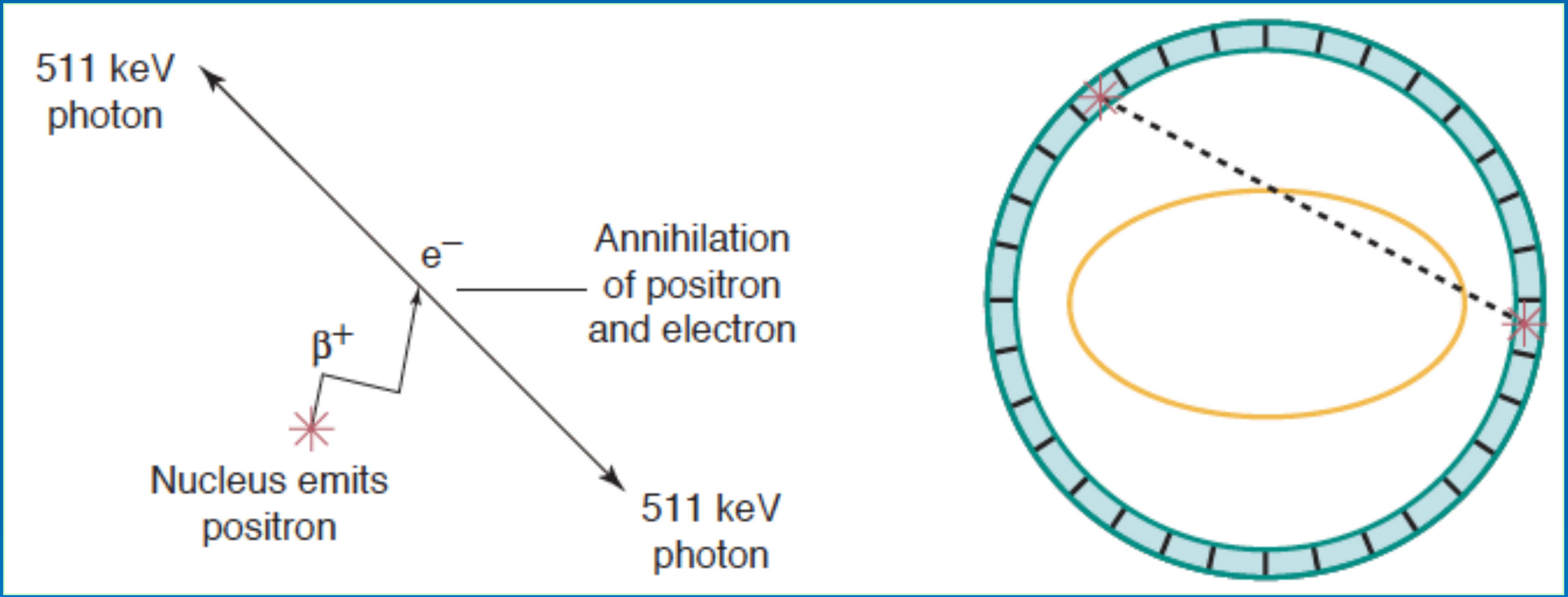
- ✓ **Positrons (β+) released from the nucleus annihilate with electrons (β-), releasing 2 coincidence 511 keV photons (γ)**
  - **which are detected by 2 detectors**
    - **blue rectangles**

N ***neutron***
P ***proton***

Kapoor et al
RadioGraphics 2004; 24:523



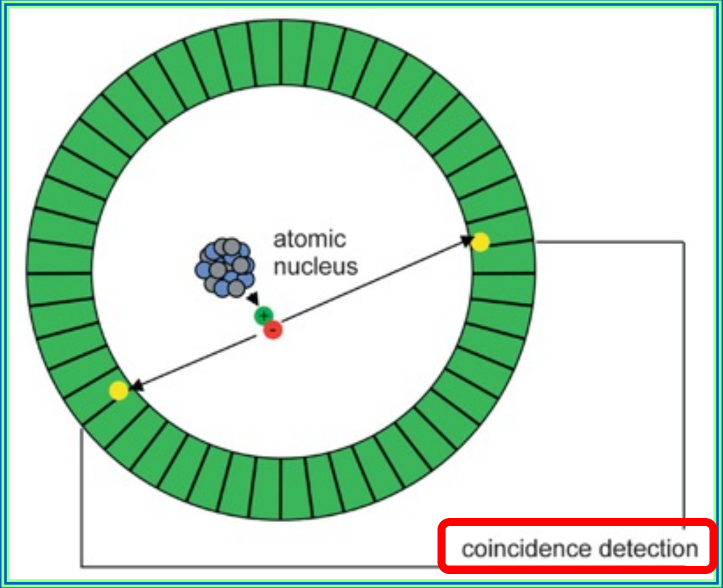
Annihilation coincidence detection

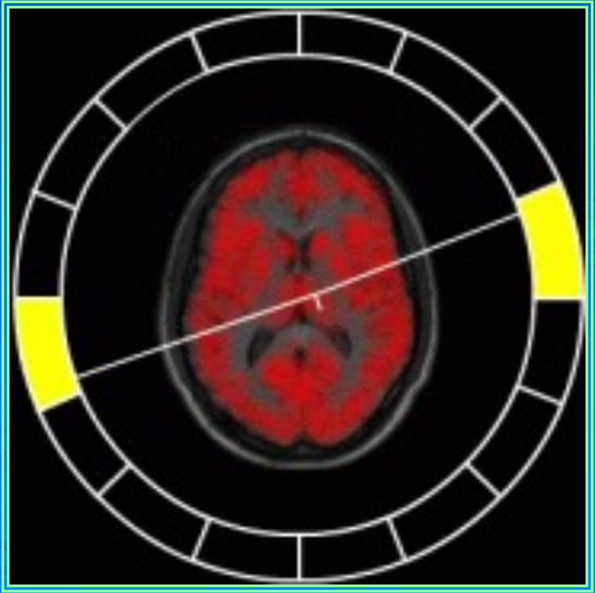


Coincidence detection allows propagation direction detection

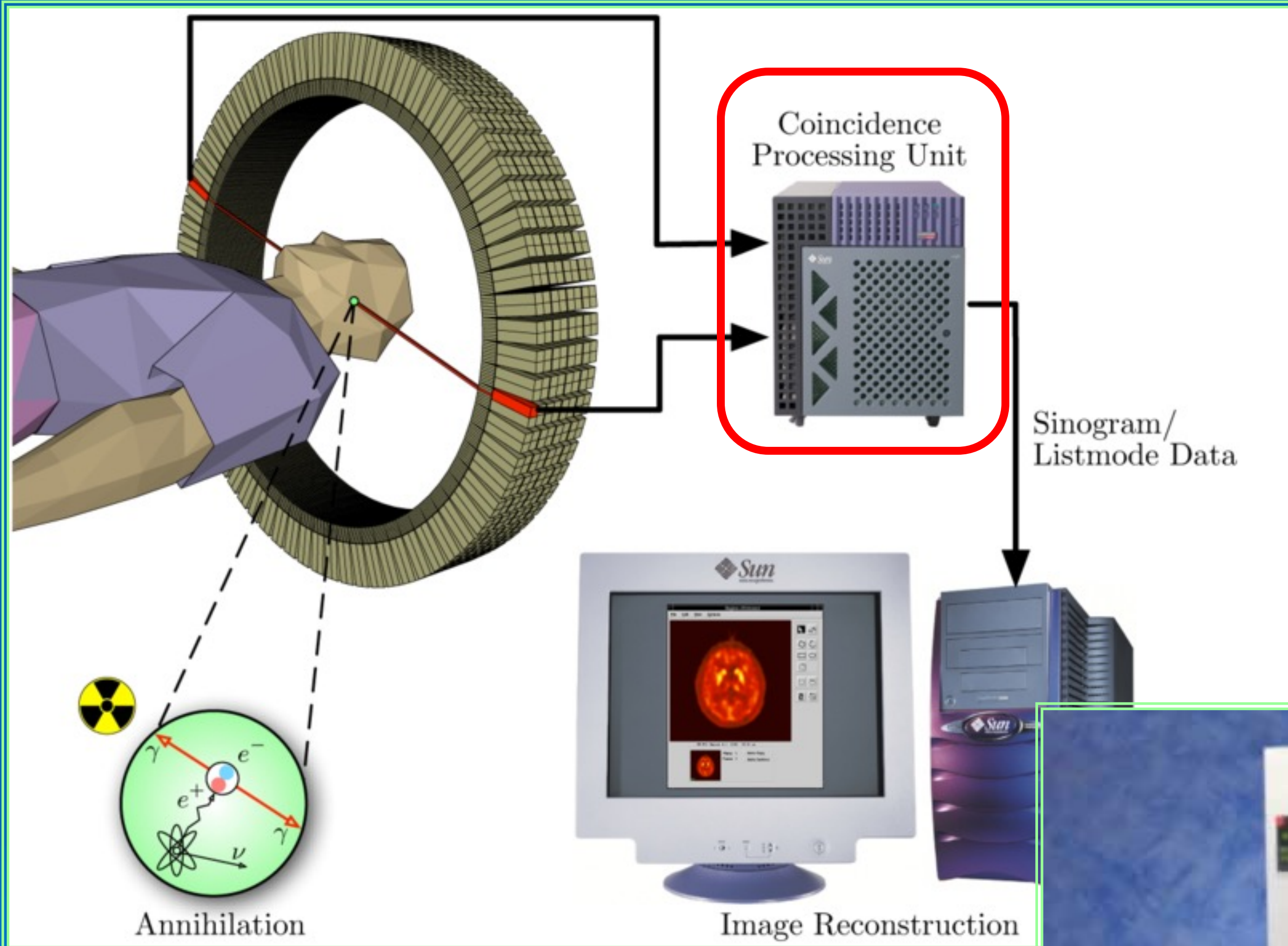
Positron Emission Tomography
PET

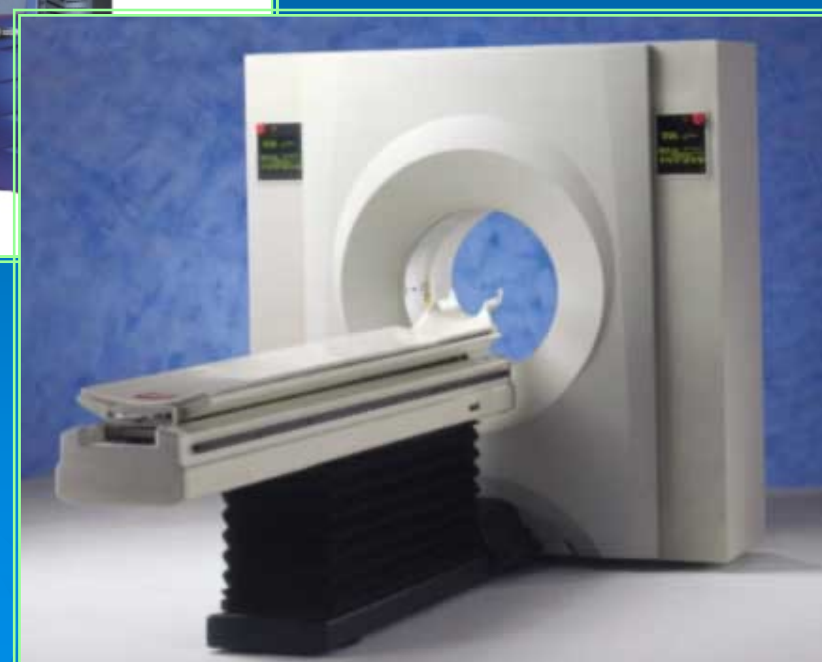
- **Process:**
  - **Injection of nuclides that emit positron**
  - **Positron annihilates on electrons**
  - **2 photons produced in exactly opposite directions**
  - **Detector that receives both photons determines position of original nuclides**
- **1-2 mm spatial resolution**





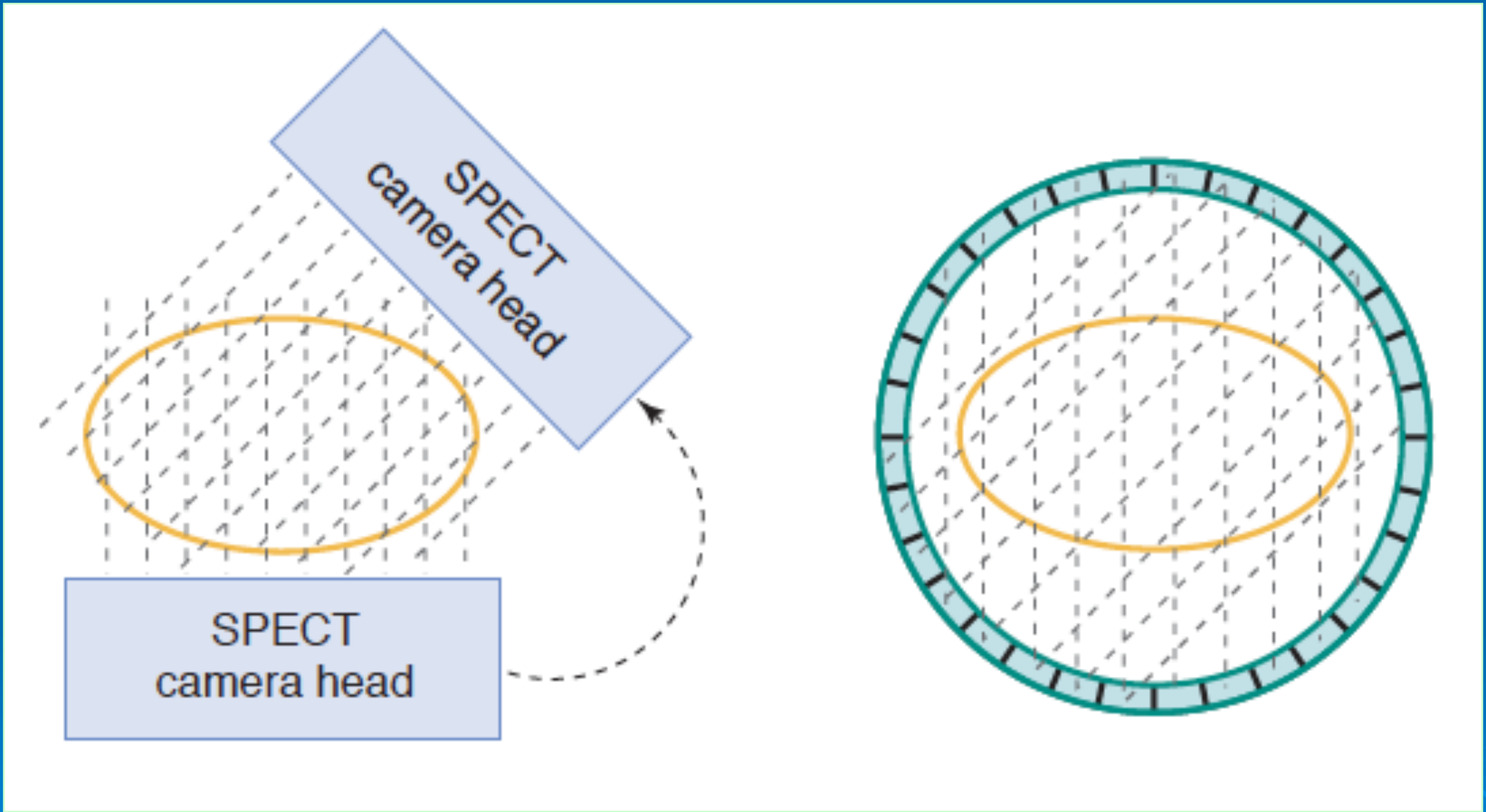
PET scanner





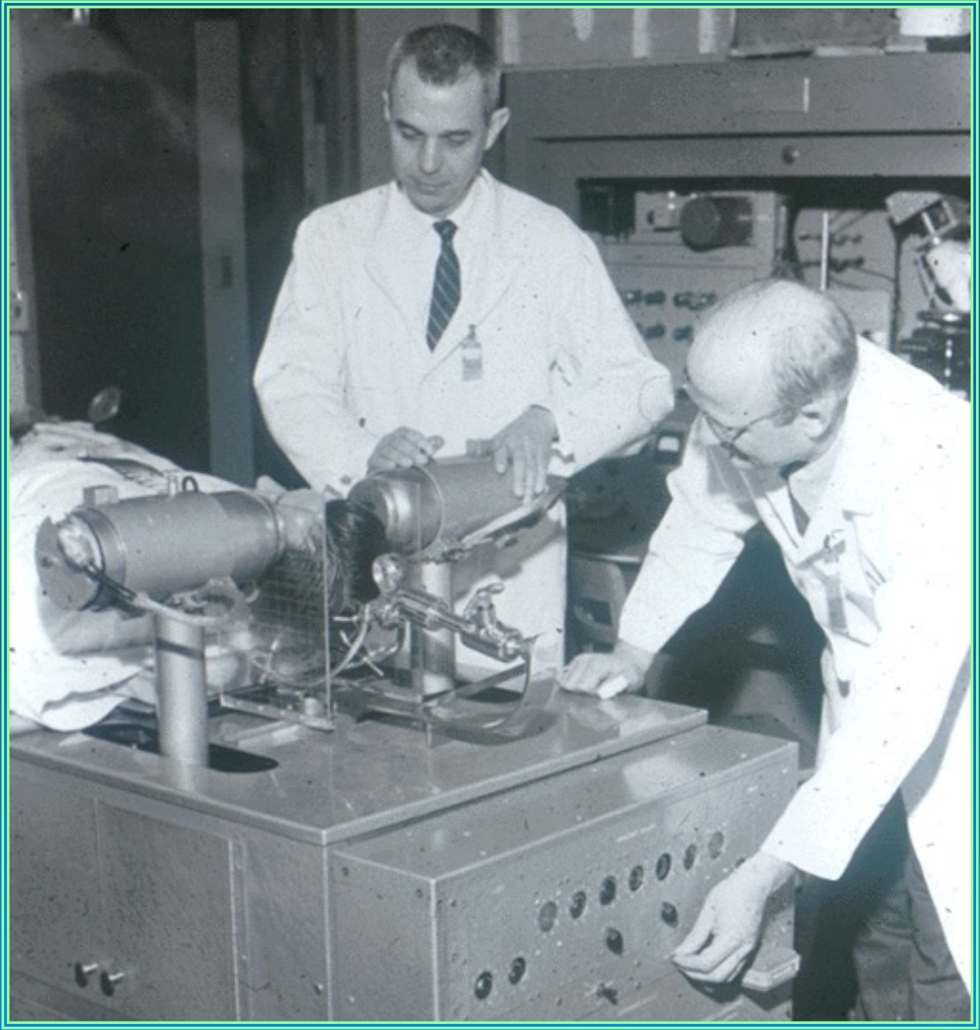
- ✓ No collimator
- ✓ The coincidence processing unit works for signal localization

SPECT vs PET



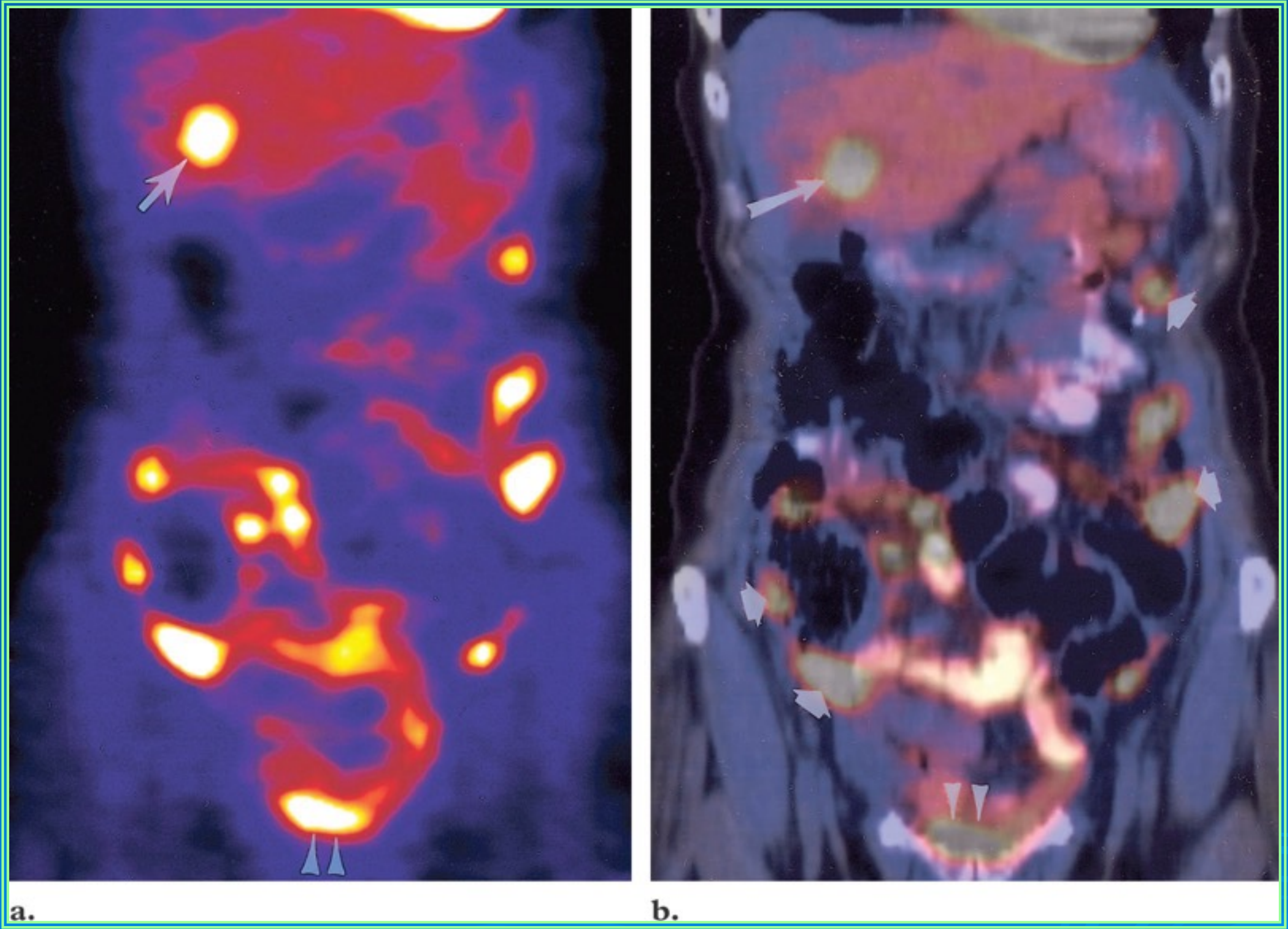
- ✓ **Coincidence detection allows propagation direction detection**
- ✓ **In PET no collimation is required:**
  Better spatial resolution and lower doses

1952: first PET acquisition



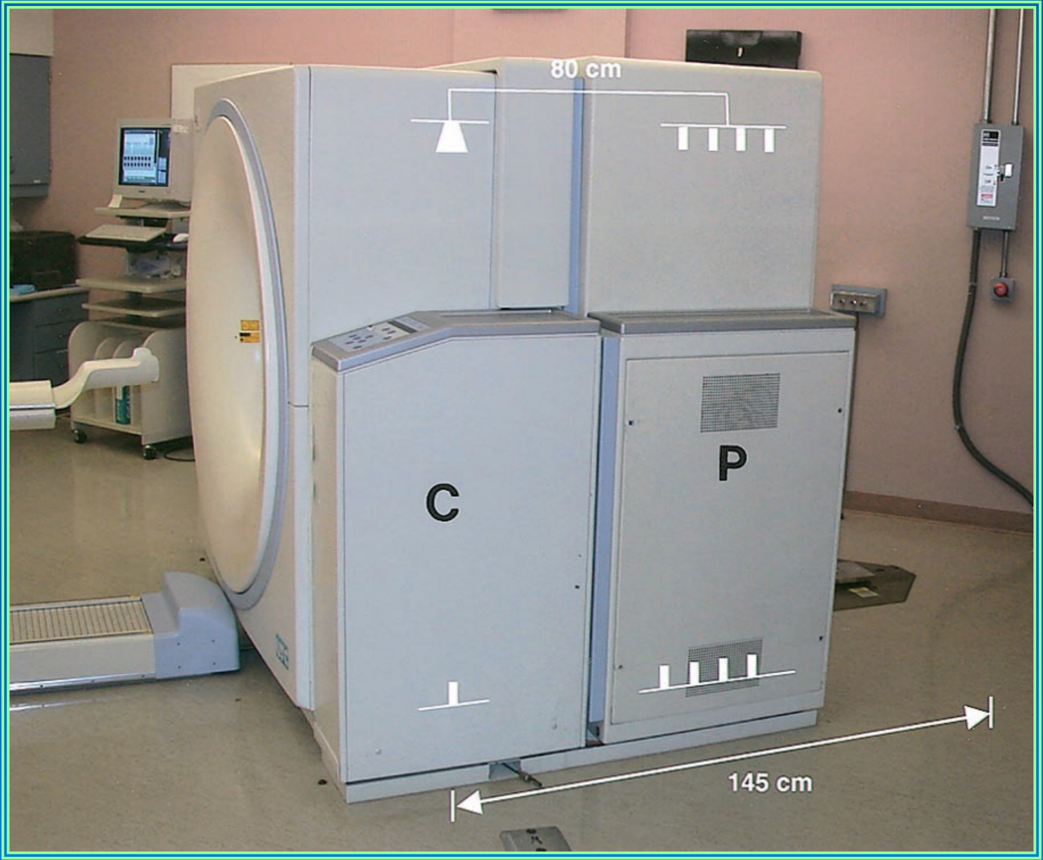
https://www.youtube.com/watch?v=qCT3KQitrCQ

Image fusion: PET & CT



An introduction to PET-CT Imaging",V. Kapoor et al, RadioGraphics 2004; 24:523–543

PET-CT systems



- the PET (P) and CT (C) components
- The PET and CT scanners are mechanically independent and can be used in isolation for PET or CT only

https://www.youtube.com/watch?v=qCT3KQitrCQ

Positron Emitting Isotopes

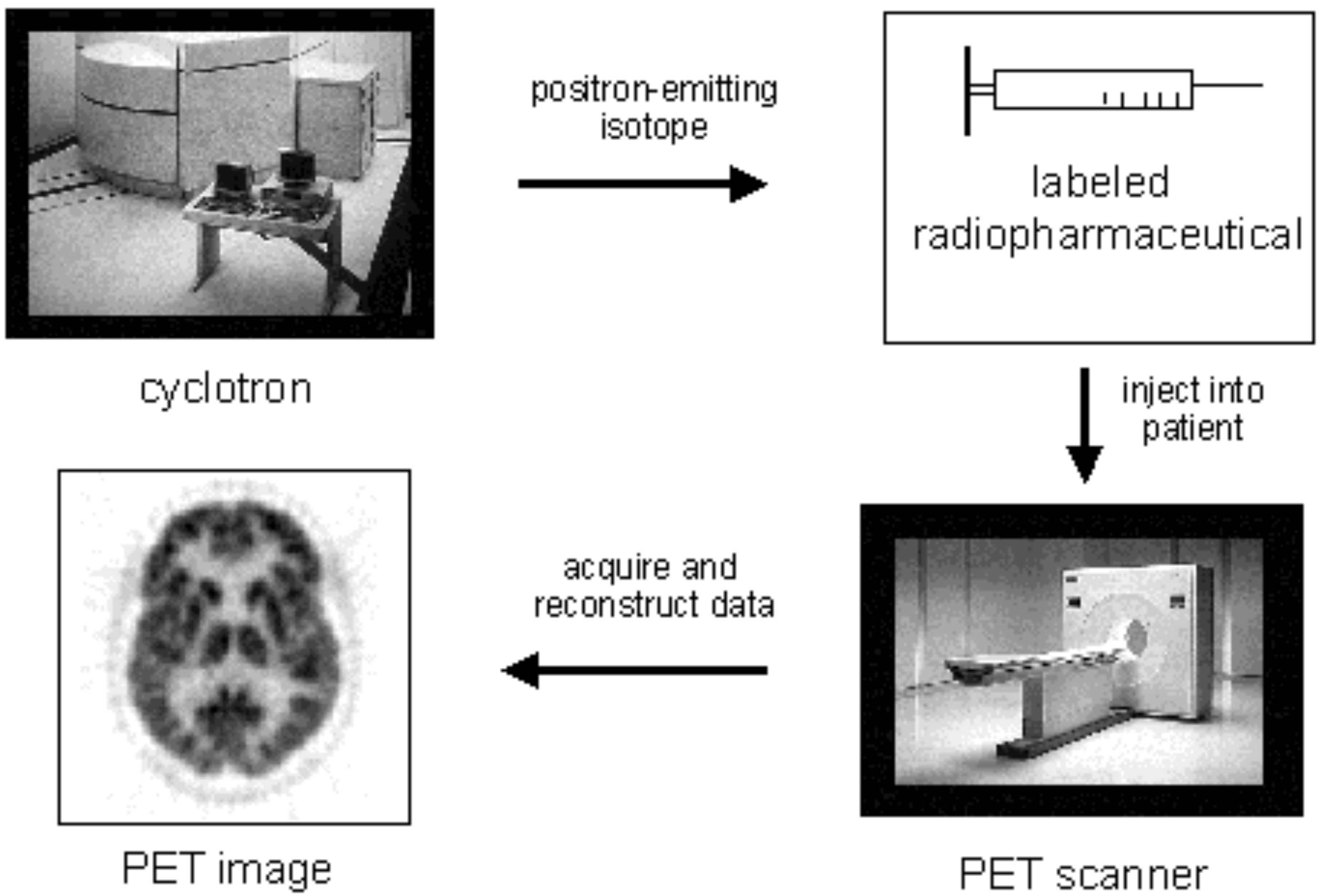
Isotope	Halflife	β^+ fraction	Max. Energy	rms(mm)
C–11	**20.4 mins**	**0.99**	**0.96 MeV**	**0.4 mm**
N–13	**9.96 mins**	**1.00**	**1.20 MeV**	**0.7 mm**
O–15	**123 secs**	**1.00**	**1.74 MeV**	**1.1 mm**
F–18	**110 mins**	**0.97**	**0.63 MeV**	**0.3 mm**
Na–22	2.6 years	0.90	0.55 MeV	0.3 mm
Cu–62	9.74 mins	0.98	2.93 MeV	2.7 mm
Ga–68	68.3 mins	0.88	1.90 MeV	1.2 mm
Rb–82	78 secs	0.96	3.15 MeV	2.8 mm
I–124	4.18 days	0.22	3.16 MeV	2.8 mm

UCLA

The cyclotron

- β+ isotopes are not available in nature
  - ^{11}C, ^{13}N, ^{15}O, ^{18}F
- They are produced on-site using a cyclotron
- $^{18}F^-$ is produced in a cyclotron by bombarding ^{18}O-enriched water with high-energy protons

Positron Emission Tomography

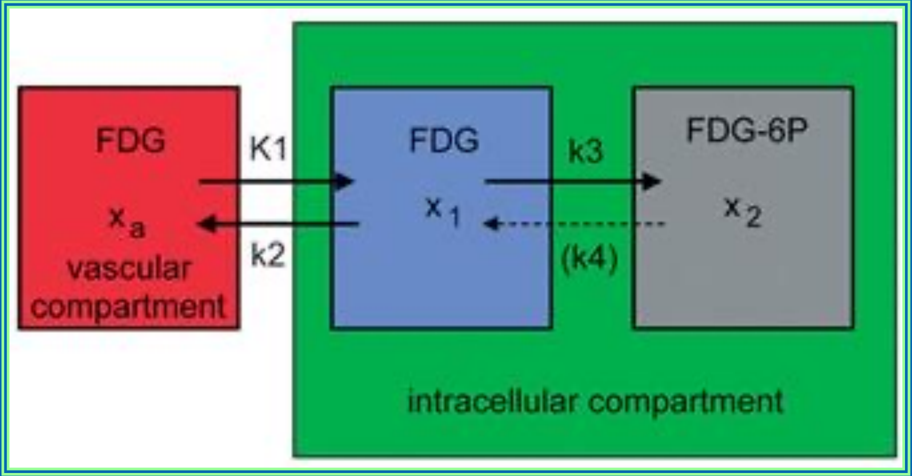


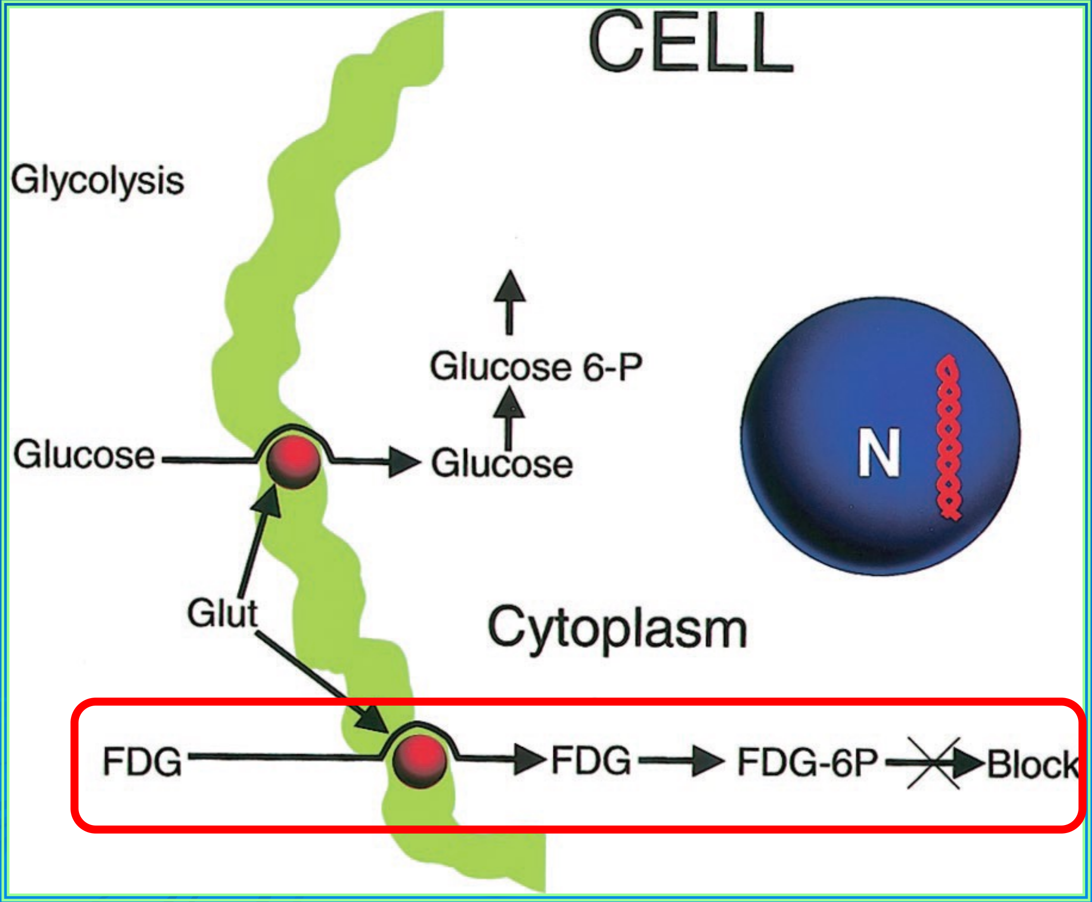
Synthesis of FDG

- Bombarding ^{18}O-enriched water with protons in the cyclotron results in a mixture of $H_2(^{18}F)$ and ^{18}O-enriched water
- Synthesis of FDG from this mixture is an automated computer-controlled radiochemical process
  - takes approximately 50 minutes to complete
- The FDG thus produced is a sterile, nonpyrogenic, colorless, and clear liquid
  - residual solvent of less than 0.04%

Uptake of FDG

- ✓ FDG is a glucose analog that is taken up by metabolically active cells via glucose transporters *(Glut)*
- ✓ In the cell cytoplasm, FDG undergoes phosphorylation to form FDG-6-phosphate
  - which cannot undergo further metabolism and becomes trapped within the cell





FDG brain imaging

- ^{18}F-FDG is the most accurate in vivo method for investigating regional human brain metabolism
- its clinical use is established for a number of diagnostic questions in neurology and psychiatry
  - dementia disorders, movements disorders
- ^{18}F-FDG PET imaging keeps an important clinical interest in epilepsy
  - particularly at inter-ictal state

Functional PET

Original methodologic approaches

- **an analysis pipeline similar to that of fMRI**
- **a constant infusion of ^{18}F-FDG defining within-session differential metabolic responses**
  - **slowly infusing ^{18}F-FDG over the course of the scan enables dynamic tracking of 18F-FDG uptake**

A Verger, E Guedj European Journal of Nuclear Medicine and Molecular Imaging (2018) 45:2338–2341

Image fusion PET MRI

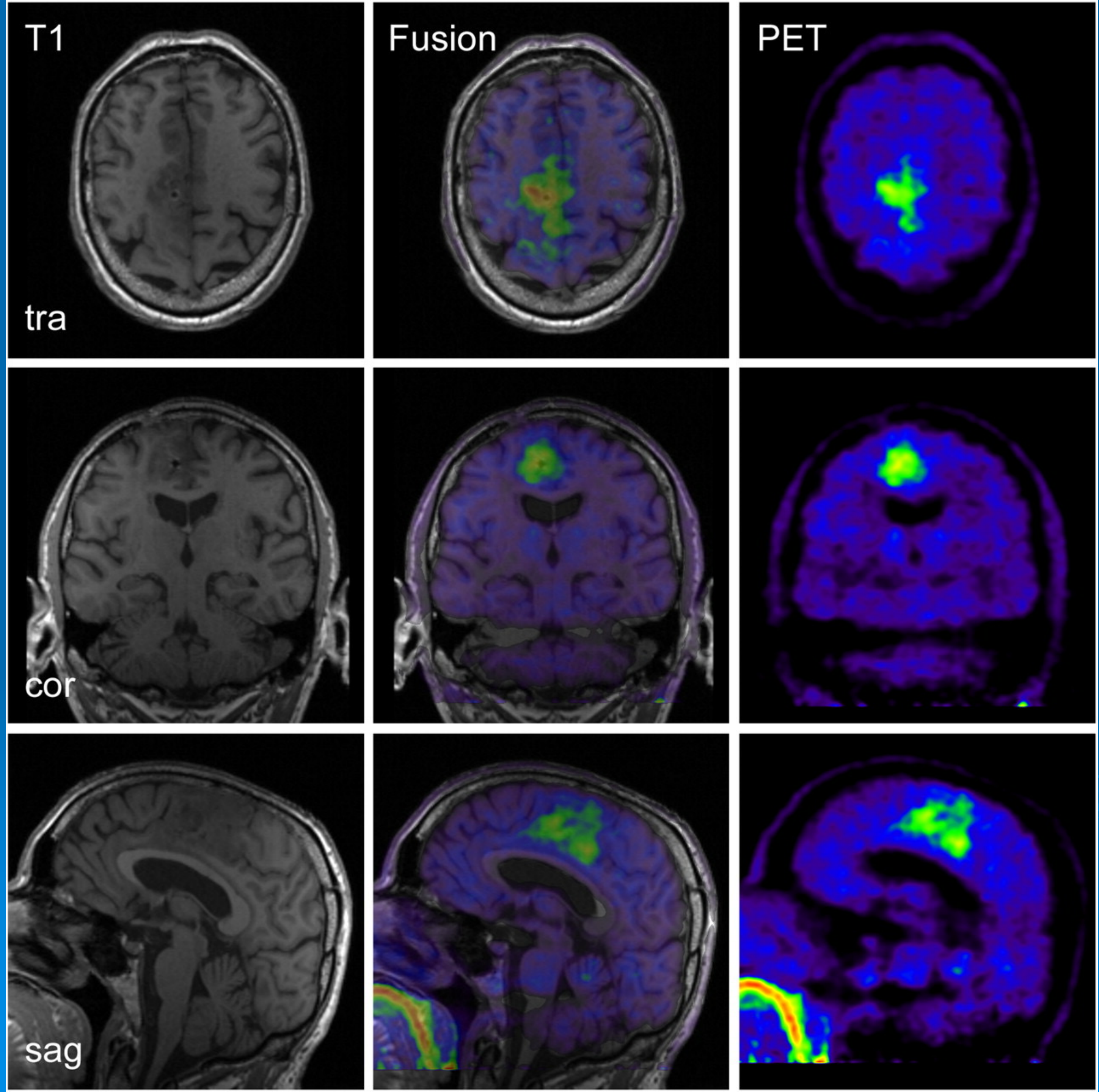
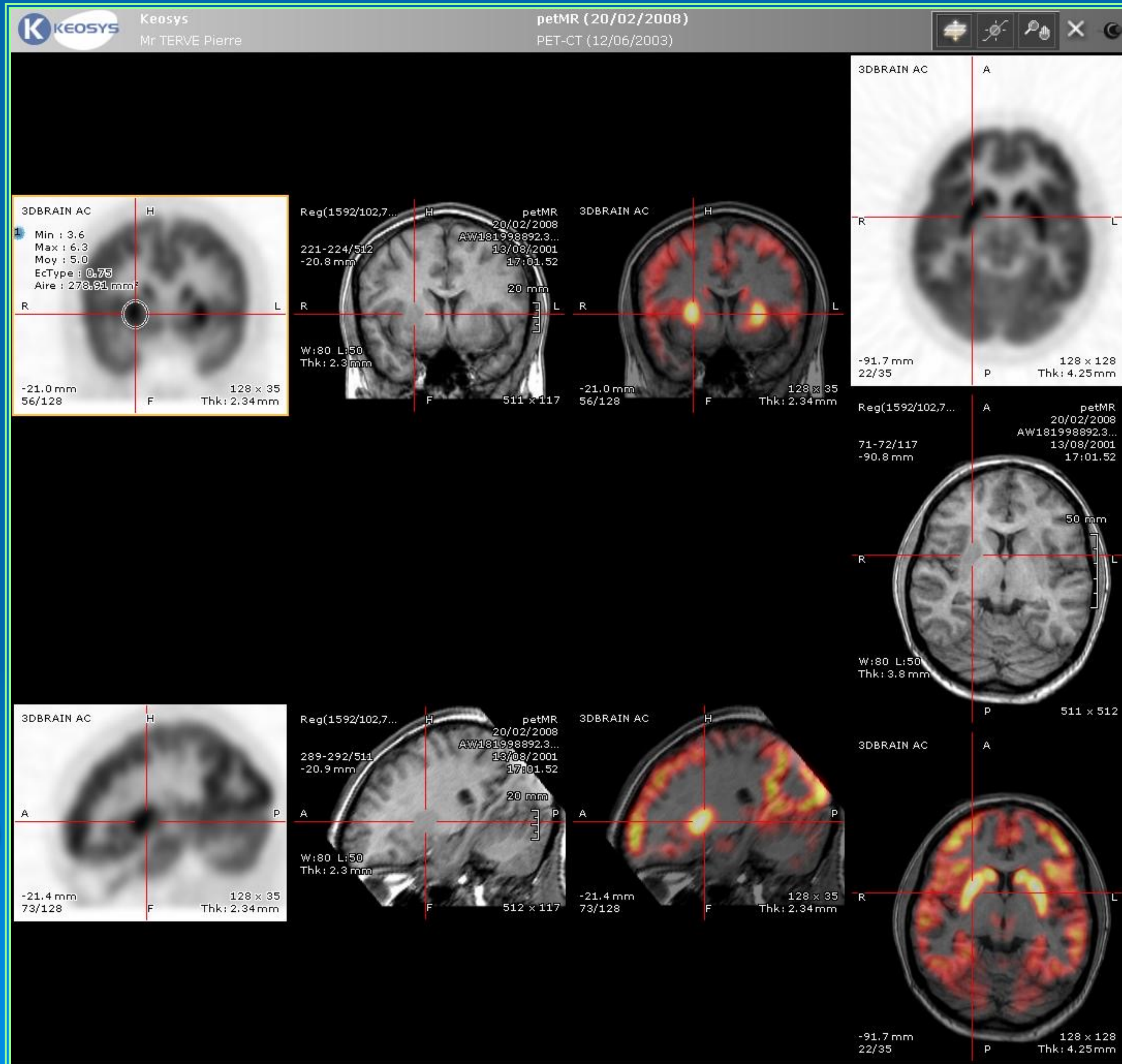


Image fusion: PET MRI



PET results

ELSEVIER

Neurobiology of Aging 30 (2009) 112–124

NEUROBIOLOGY OF AGING

www.elsevier.com/locate/neuaging

Voxel-based mapping of brain gray matter volume and glucose metabolism profiles in normal aging

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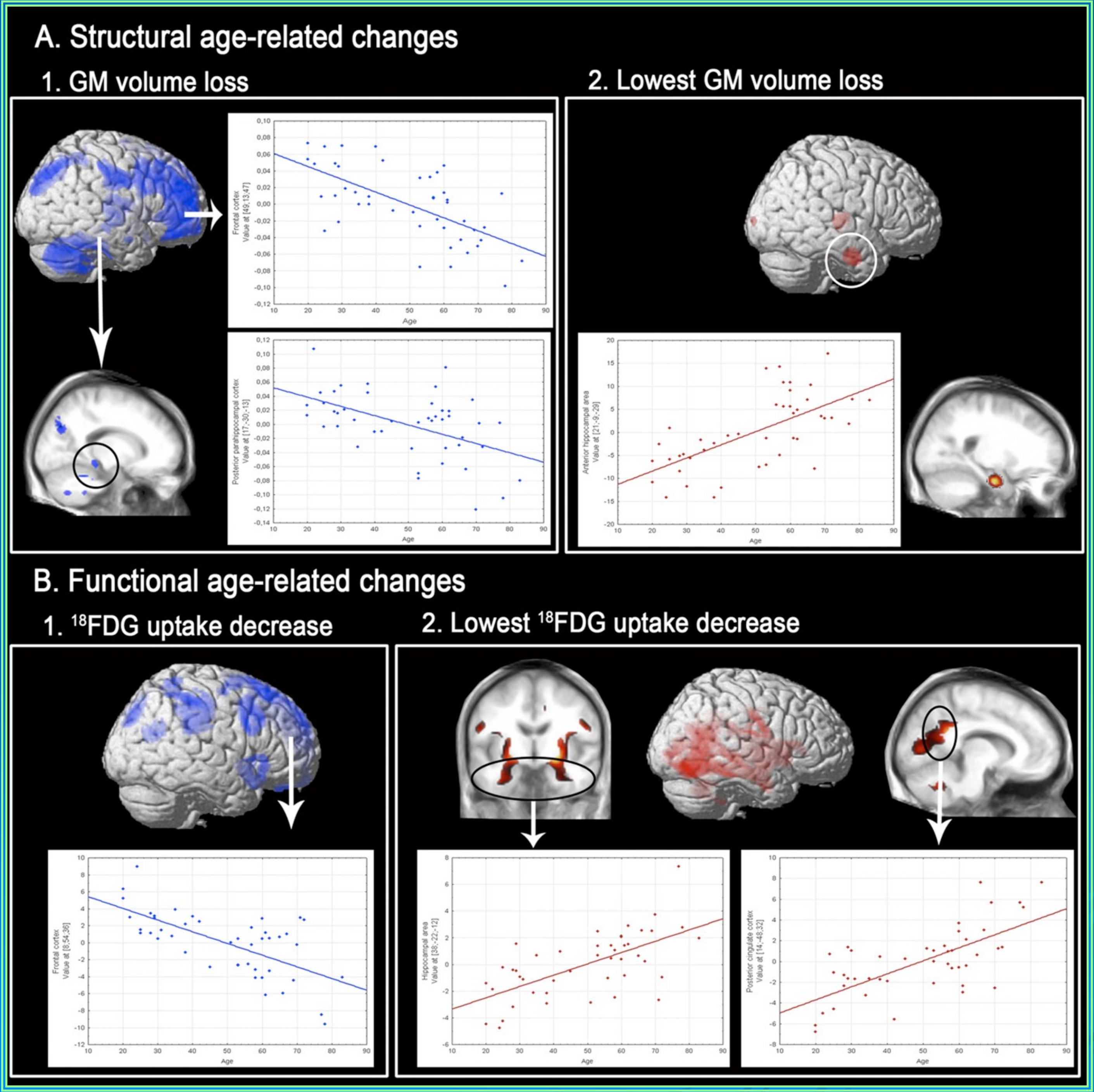
PET results


A. Structural age-related changes
1. GM volume loss
2. Lowest GM volume loss
Frontal cortex
Value at [49;13;47]
Posterior parahippocampal cortex
Value at [17;-30;-13]
Anterior hippocampal area
Value at [21;-9;-29]
Age
B. Functional age-related changes
1. 18FDG uptake decrease
2. Lowest 18FDG uptake decrease
Frontal cortex
Value at [8;54;36]
Hippocampal area
Value at [38;-22;-12]
Posterior cingulate cortex
Value at [14;-48;32]
Age

Brain PET substrate of impulse control disorders in Parkinson's disease: A metabolic connectivity study

Hum Brain Mapp. 2018;39:3178–3186.

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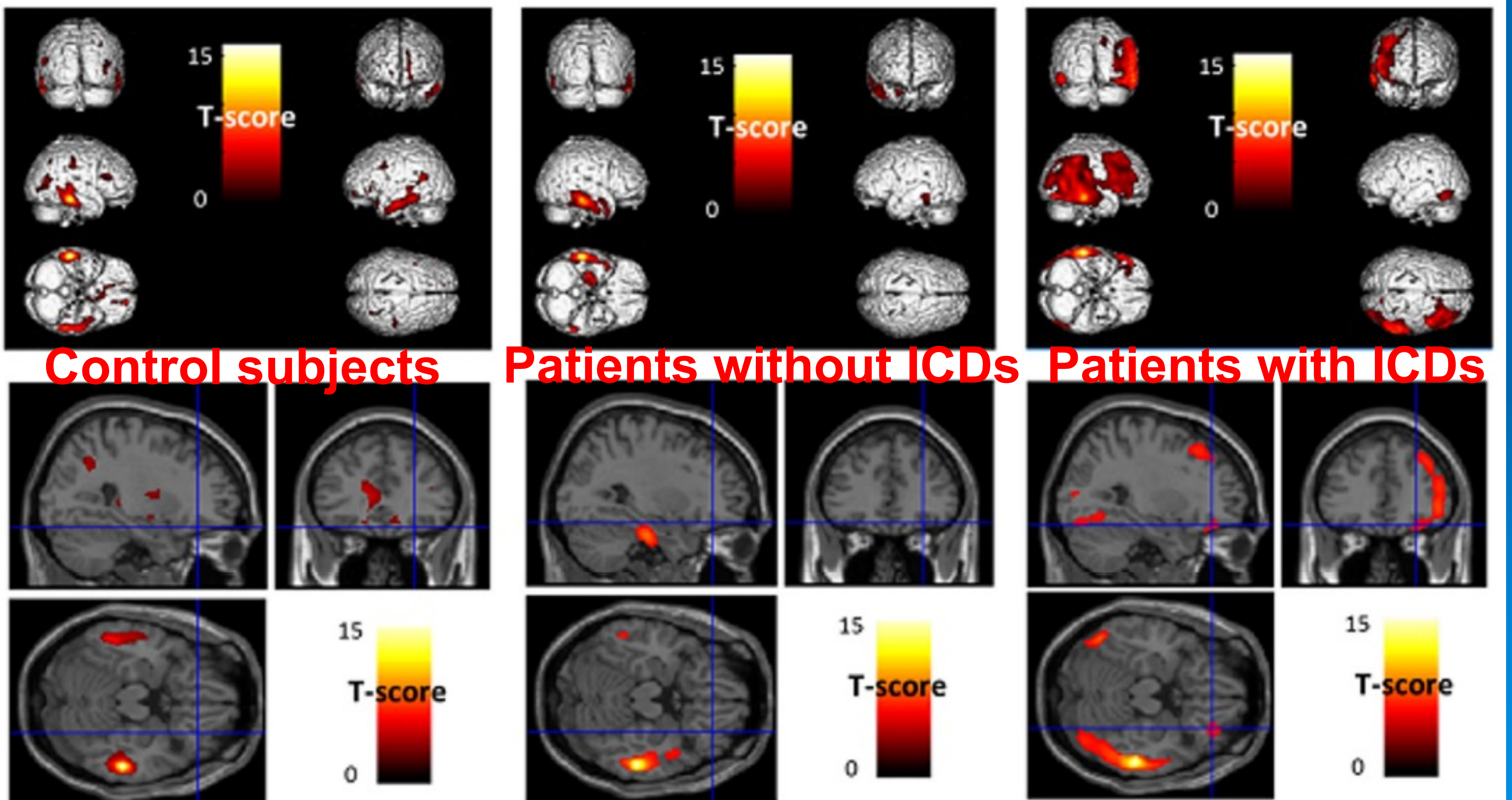
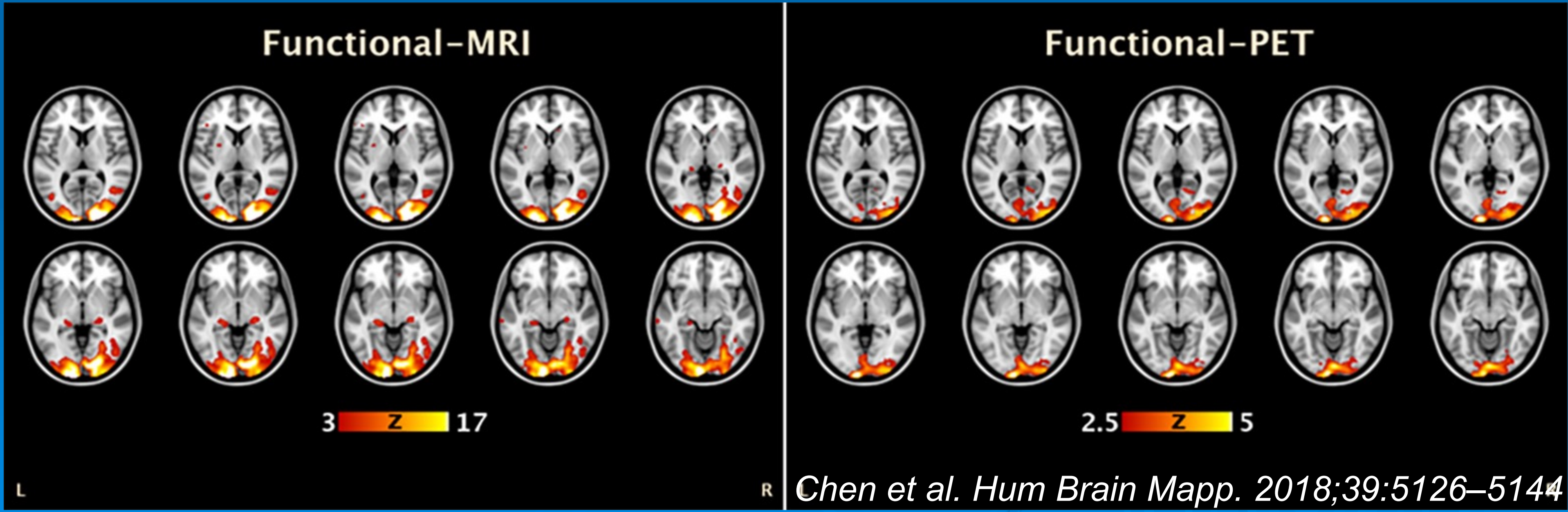


PET/MR systems

the multimodality approach integrates functional connectivity obtained with fMRI with the PET data

- **potential complementarity offered by both modalities**

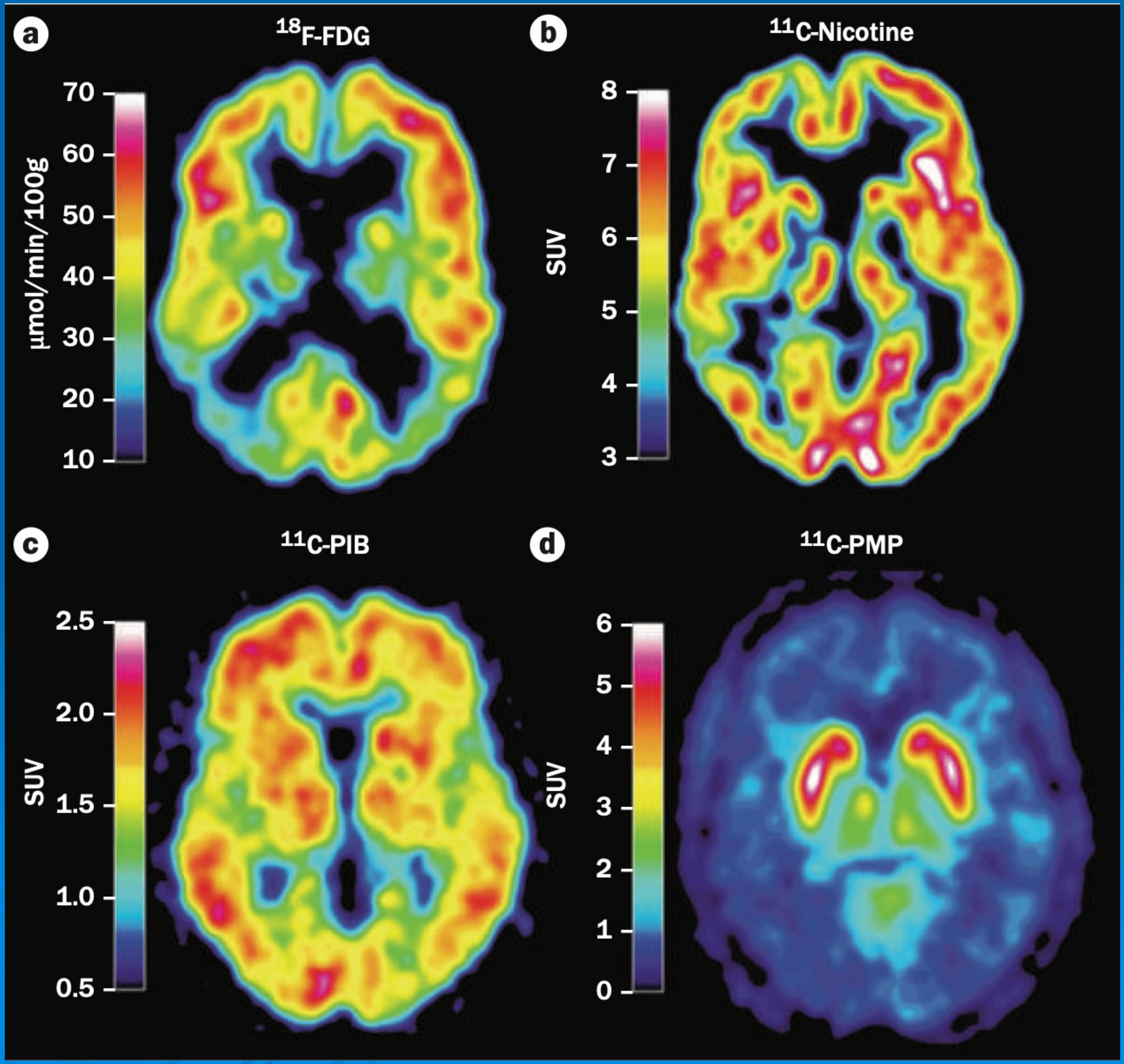


Chen et al. Hum Brain Mapp. 2018;39:5126–5144

The results are comparable, but with more focused activity in the FDG-fPET than BOLD-fMRI data

Amyloid PET Scan for Alzheimer's Disease Assessment

New tracers for dementia studies



Nordberg, A. et al. (2010) Nat. Rev. Neurol. 6, 78–87