

Nuclear neurology



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To refresh your memory

- Brain has a **high rate of oxidative metabolism**. It has **no reserves** either of **oxygen** or of **glucose** and has a very limited capacity for anaerobic metabolism. Therefore normal **brain function** is critically **dependent on** maintenance of an adequate **blood supply**. There is a linear association between glucose metabolism and functional activity of the brain.
- Normal cerebral blood perfusion: 50-60 ml/min/100g
- Cortex: 65-85 ml/min/100g
- White matter: 25-35 ml/min/100g
- **No EEG activity: below 17 ml**
- **Failure of Na/K ATP-ase: below 10 ml**

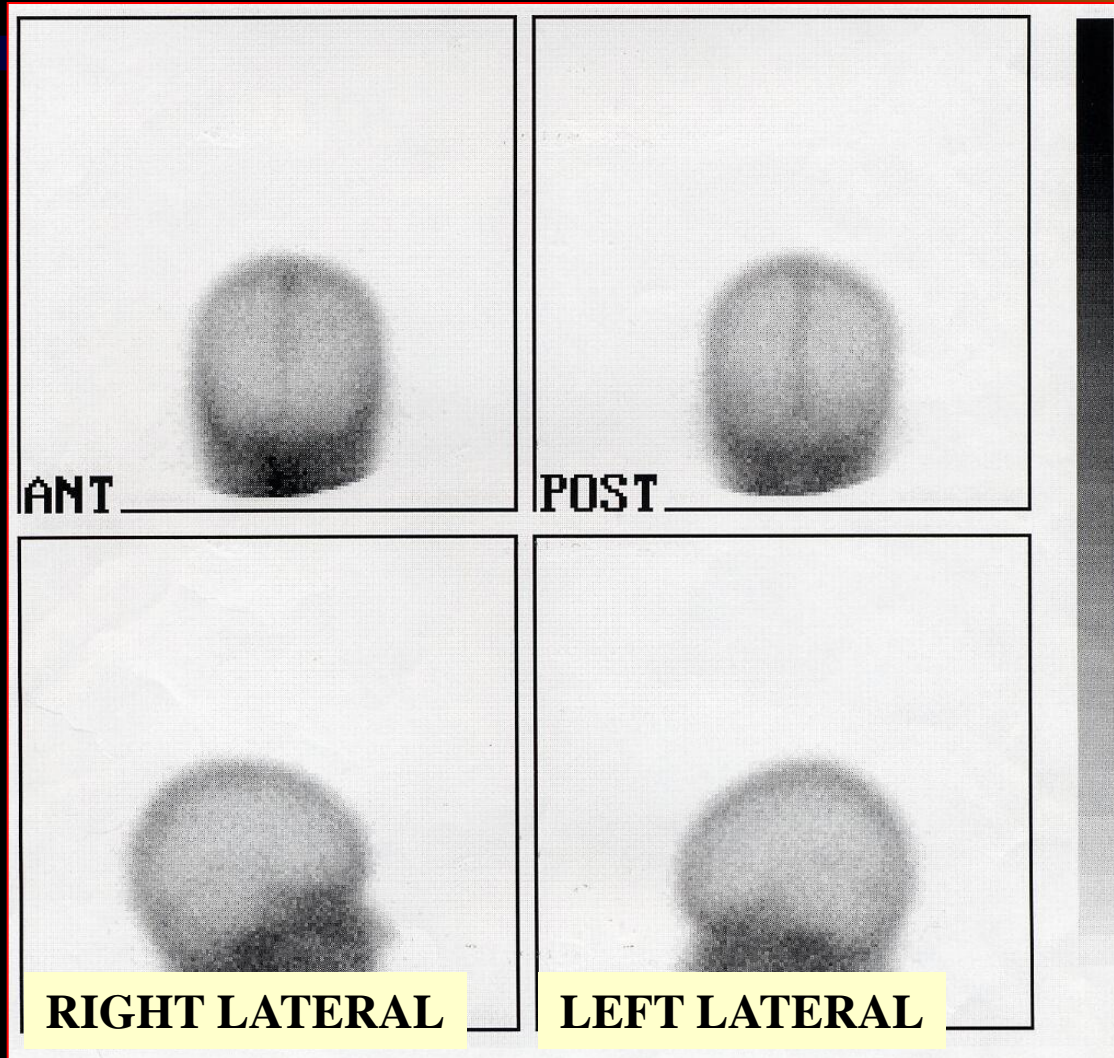
Methods

- **Brain scintigraphy** - damaged blood-brain barrier (BBB)
- **Brain perfusion study** - vascular lesions (SPECT/CT)
- **Examination of cerebrospinal fluid (CSF)** - (dynamics, liquorrhoea)
- **Receptor studies** - gamma or positron emitting isotopes (SPECT/CT, PET/CT)
- **Glucose-, aminoacid metabolism, quantitative CBF examination** (PET/CT)

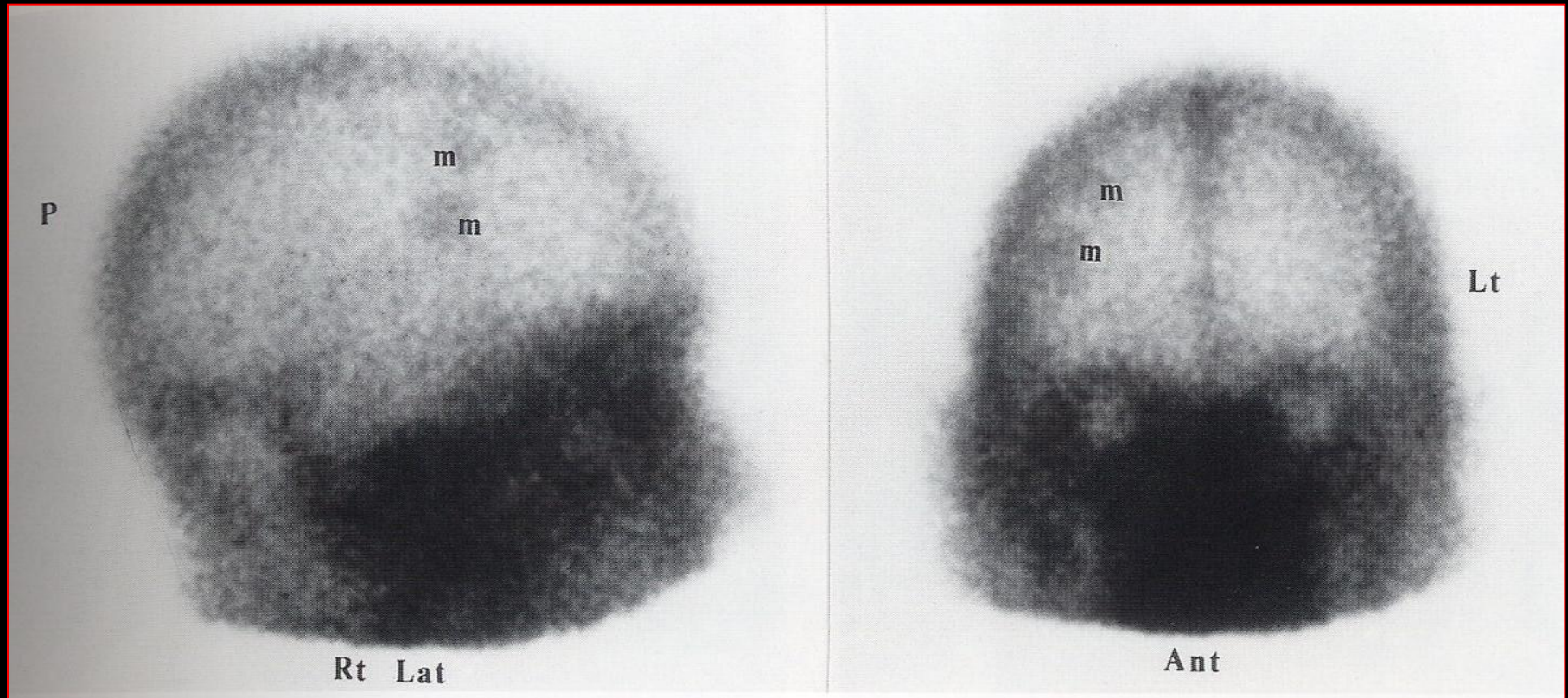
Brain scintigraphy

- **Blood-brain barrier (BBB):** lipid-protein double layer
- protective function
- **Radiopharmaceutical:** 500-750 MBq ^{99m}Tc -DTPA
i.v., 40 min. waiting
- 4 projection - static scans (A, P, right, left) + combined
with SPECT or SPECT/CT scan (dual-head SPECT)
- **Abnormalities of permeability** indicate disruption of
BBB (tumor, vasculare lesion), but CT and MR with
contrast show more detailed anatomical correlations
- **Historical role:** confirmation of brain death

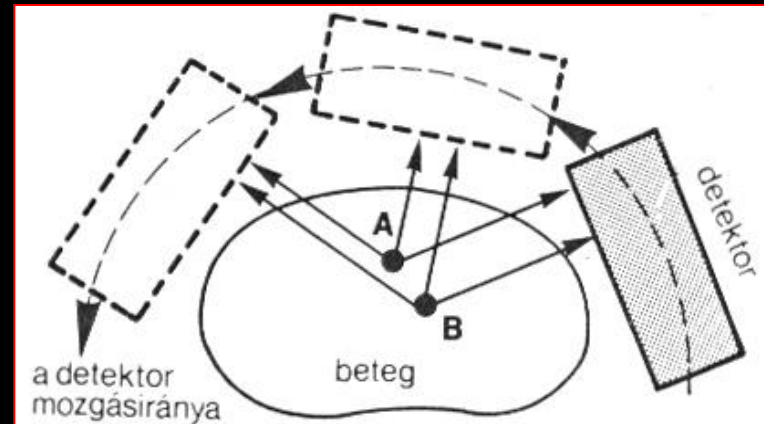
Normal brain scintigraphy



Cerebral metastases in the right hemisphere



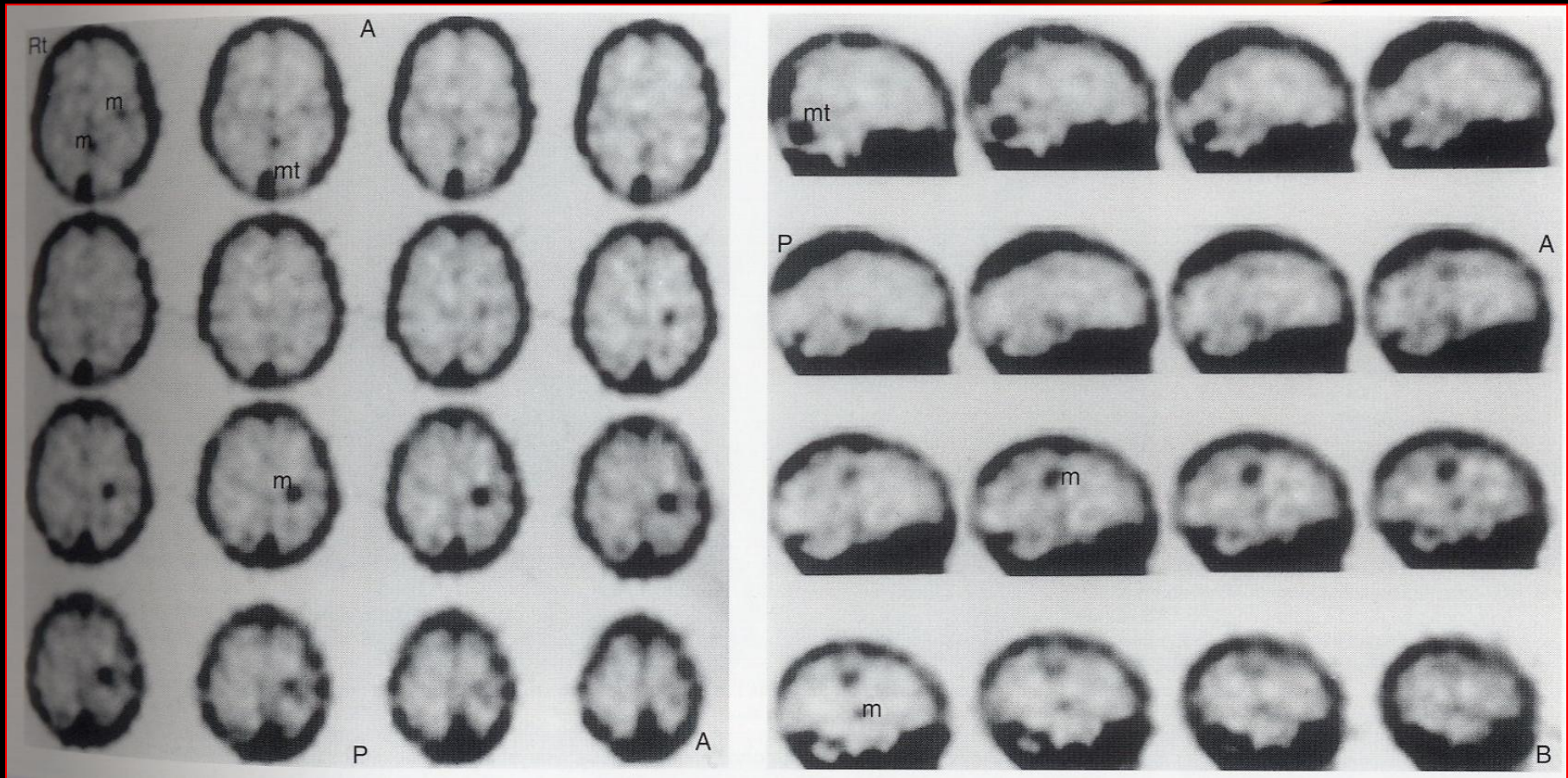
SPECT (Single Photon Emission Computer Tomograph)



The transversal, sagittal and coronal slices of the organ are reconstructed and reorientated by the computer program.

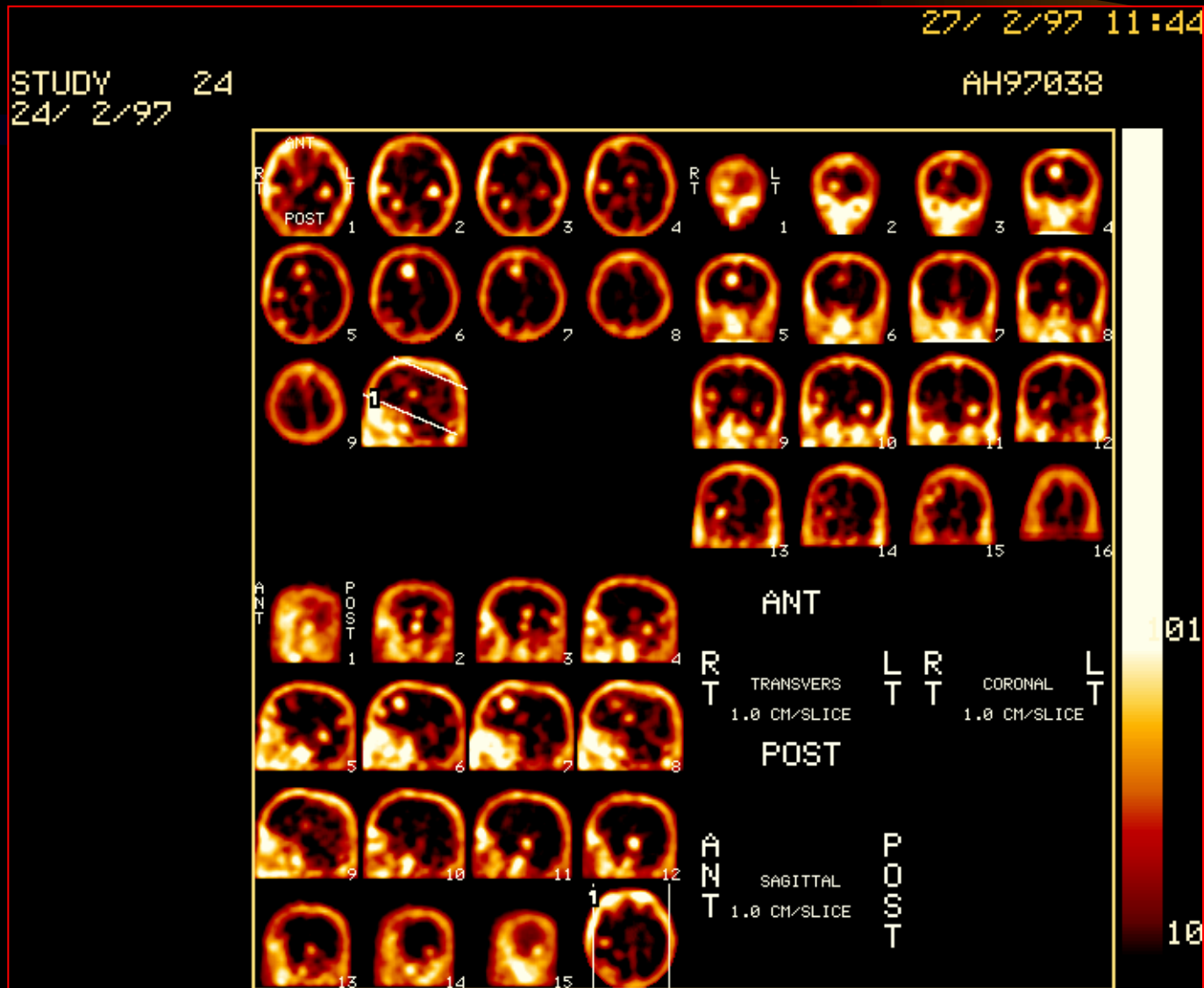
Multiple metastatic lesion in the left hemisphere of the brain

SPECT scan

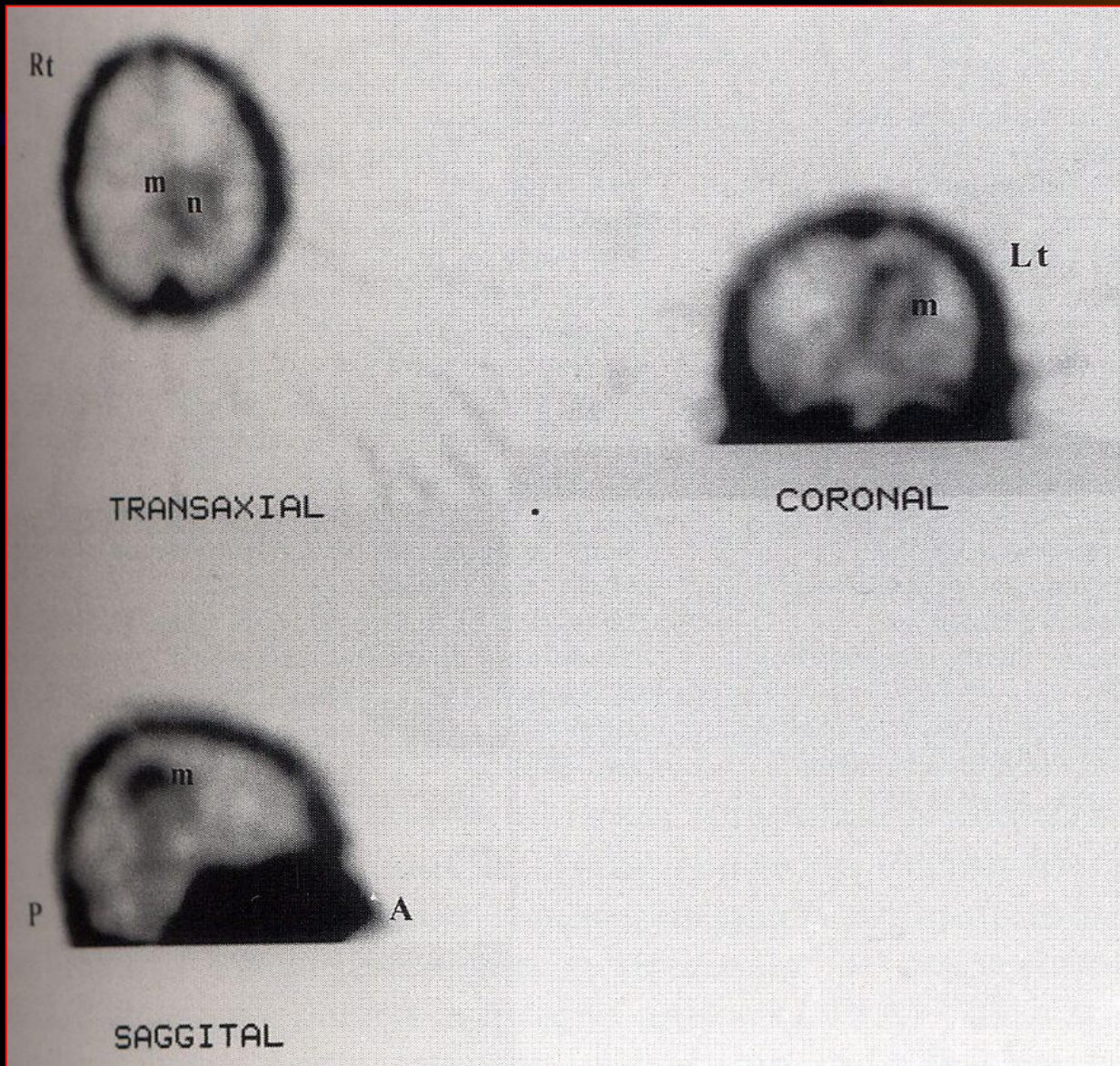


Multiplex brain metastases in melanoma malignum

SPECT imaging



Cerebral embolisation in the left hemisphere



**SPECT
scan**

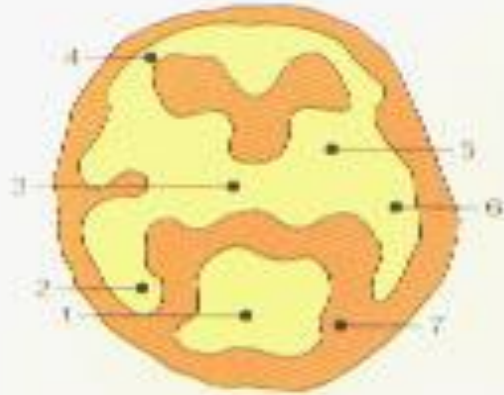
Cerebral blood flow and perfusion

- Lipophilic tracer is enriched **in the gray matter** (800 MBq ^{99m}Tc -HM-PAO – hexamethylpropylene amine oxime)
- Advantage of **dual-head SPECT** = faster acquisition
- Reconstructed and reorientated transversal, sagittal and coronal slices are made
- **Decreased/absent activity** indicates the perfusion abnormalities

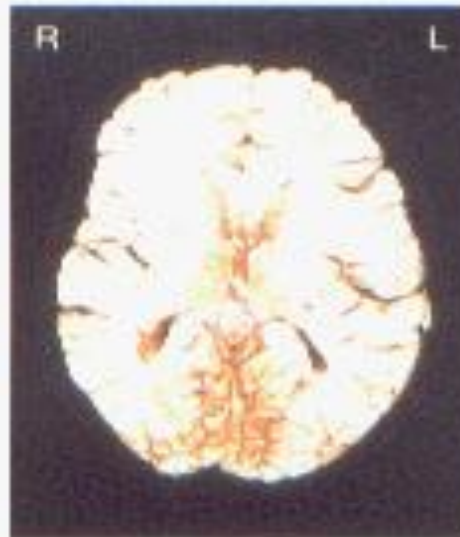
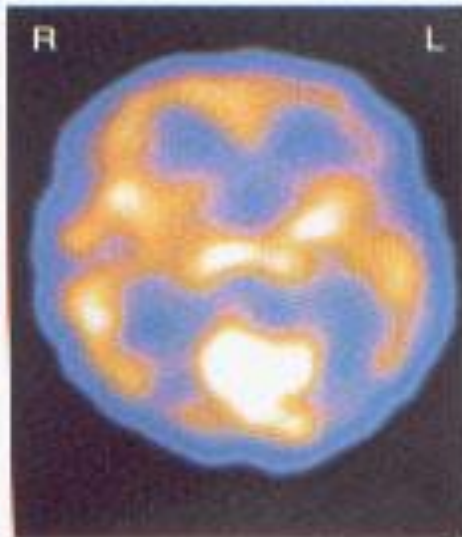
Indications of CBF SPECT

- **Evaluation of cerebrovascular disease (TIA, stroke, AVM, migraine)**
- **Dementias (Alzheimer, Pick)**
- **Preoperative detection of seizure focus in epilepsy**
- **Suspected brain trauma**
- **Substance abuse**
- **Inflammations, infections**
- **Diagnosis of brain death**

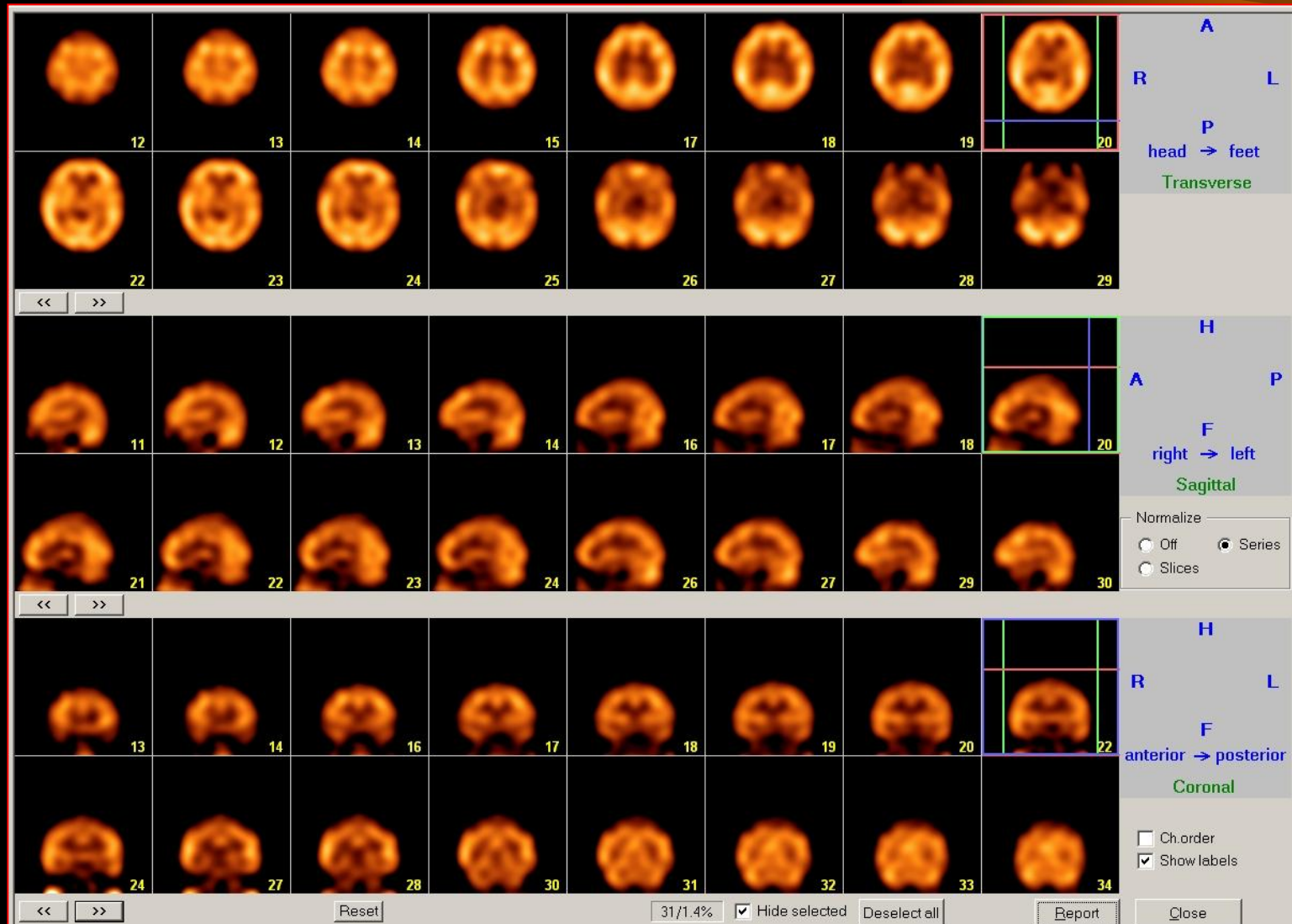
Transversal section of the human brain



1. Visual cortex
2. Occipital lobe
3. Thalamus
4. Frontal lobe
5. N. caudatus
6. Temporal lobe
7. Lateral ventricle

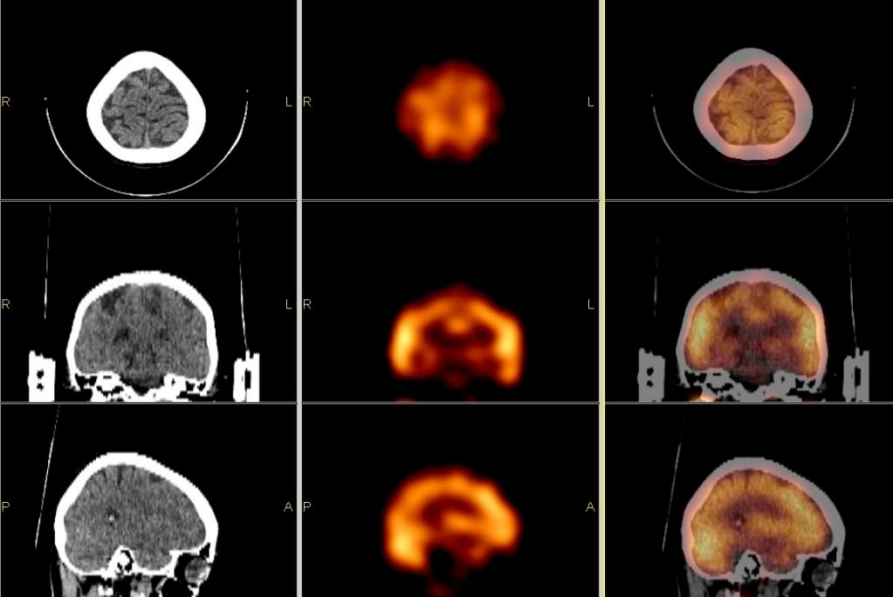


Transversal, sagittal and coronal slices of the normal brain by SPECT

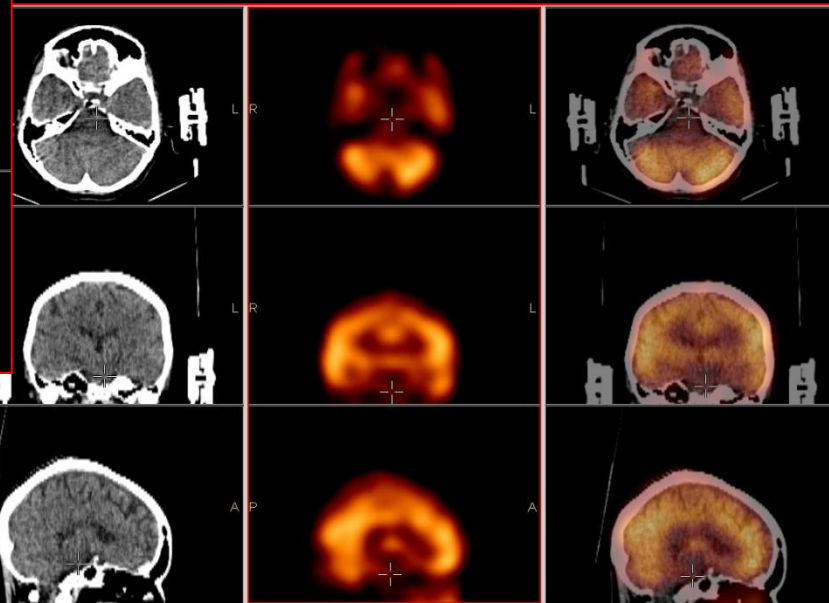
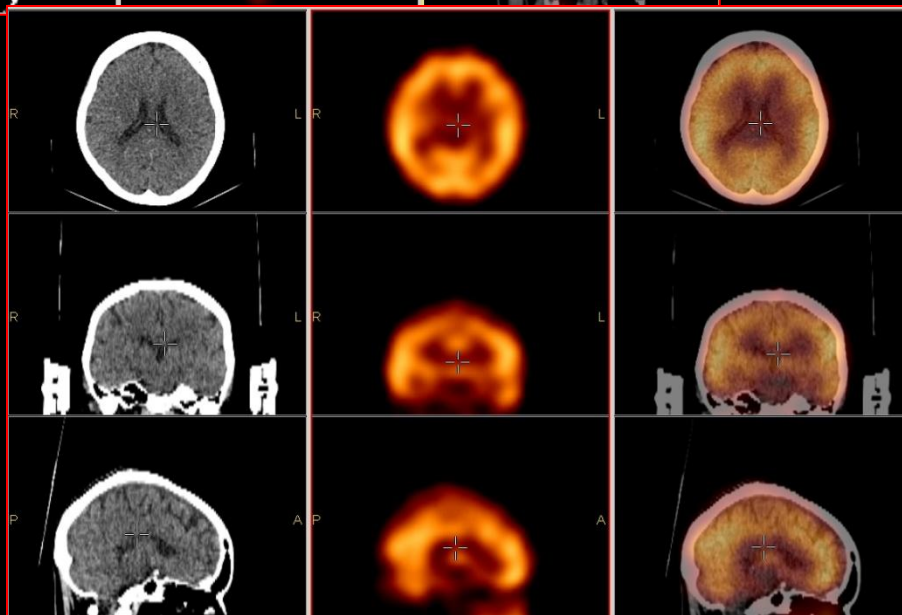


SPECT/CT (Multimodality!)

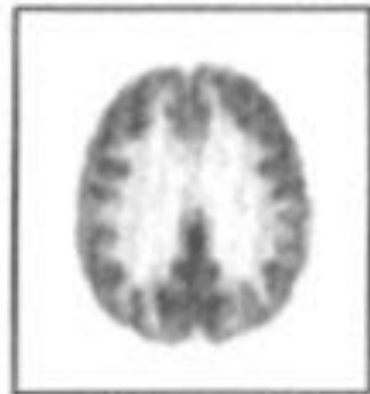




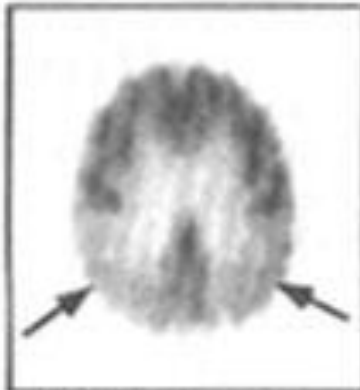
Different slices of the brain by SPECT/CT



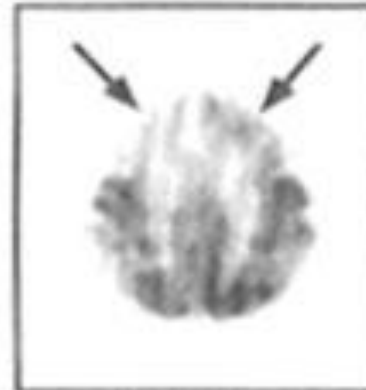
Perfusion abnormalities in different brain disorders



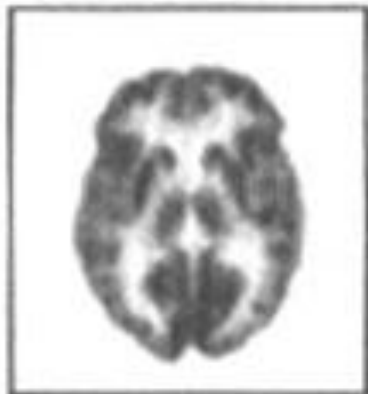
Normal



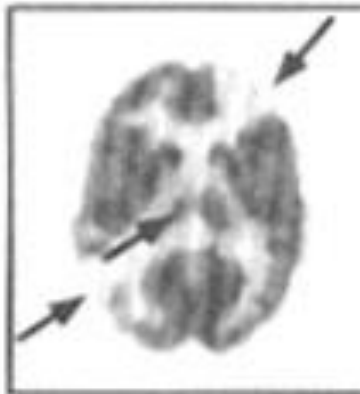
Alzheimer's



Pick's



Normal

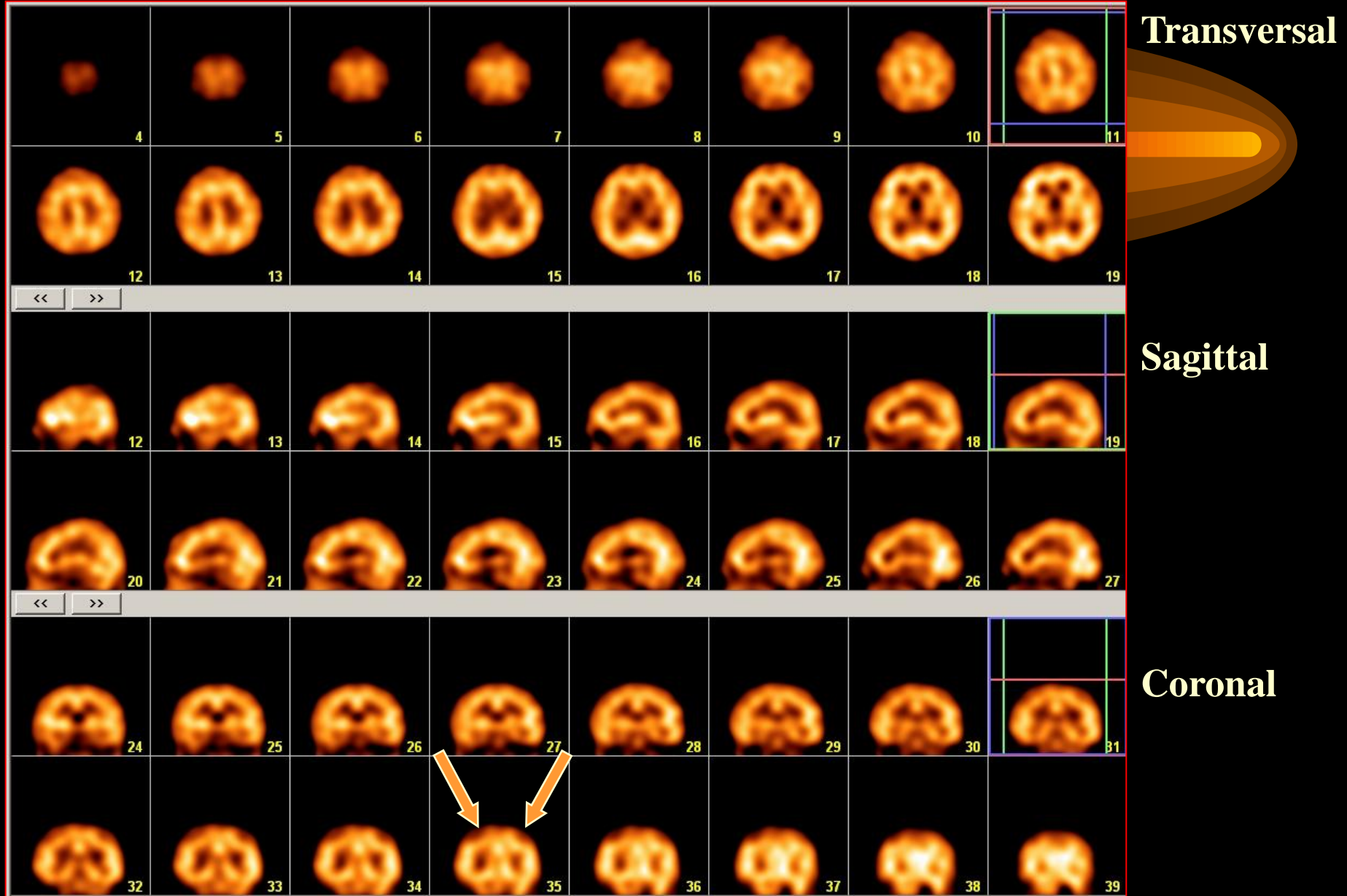


Multiple Infarct
Dementia

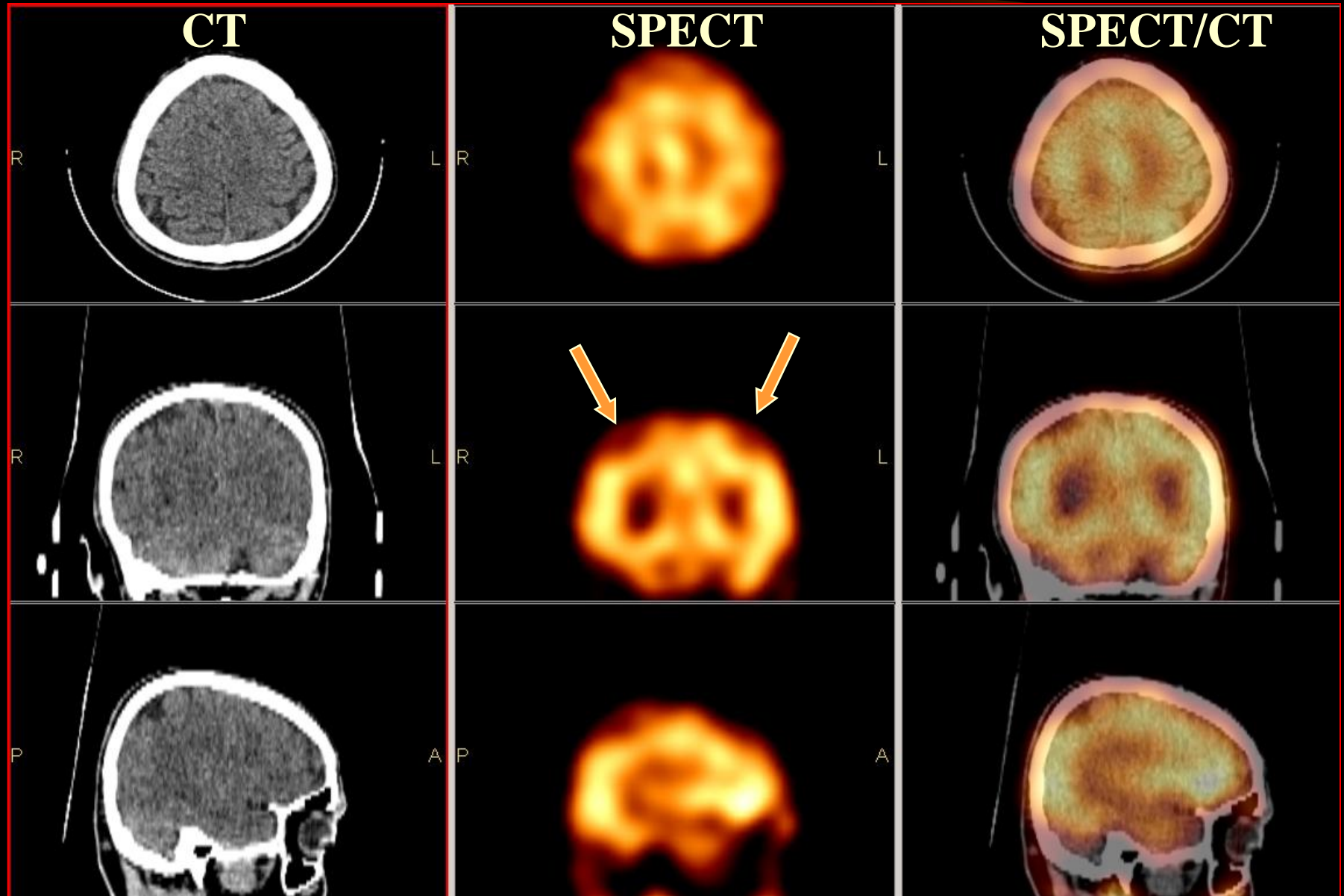


Huntington's

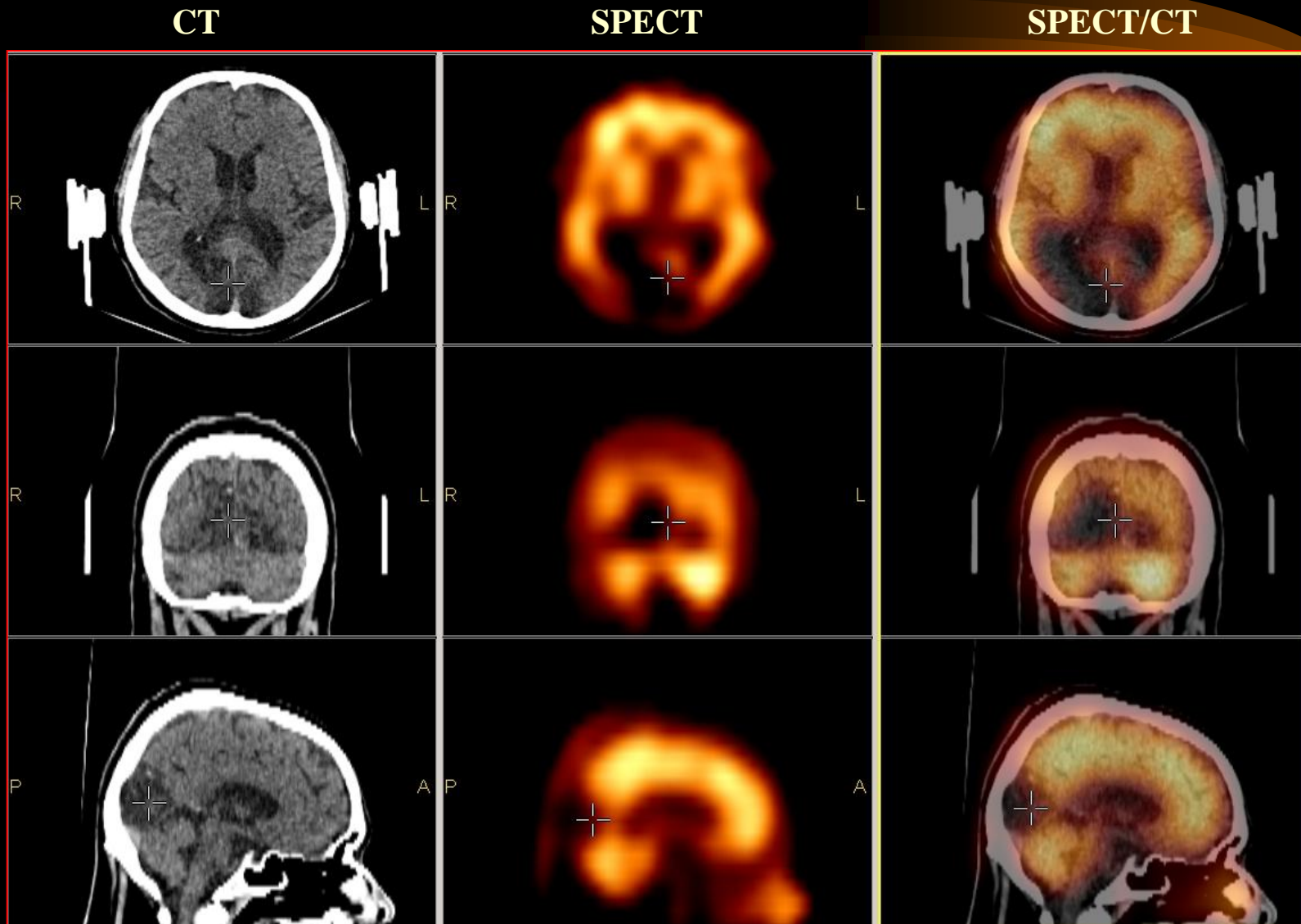
Bilateral parieto-occipital hypoperfusion



Bilateral parieto-occipital hypoperfusion



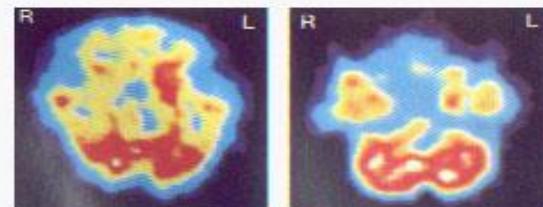
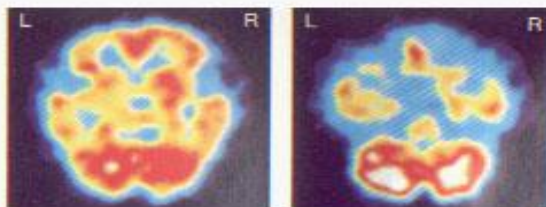
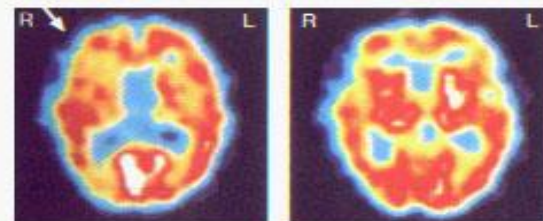
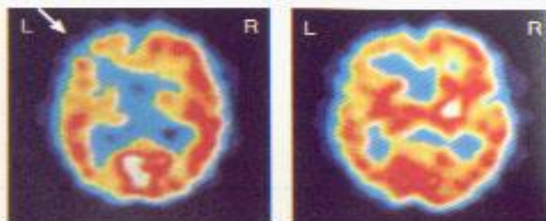
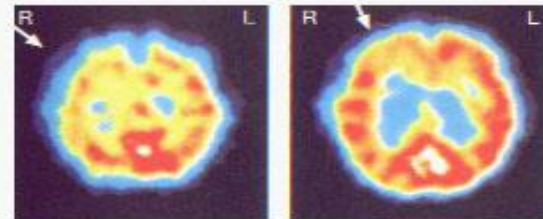
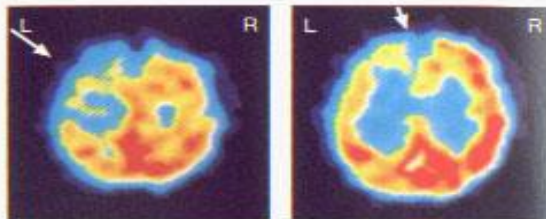
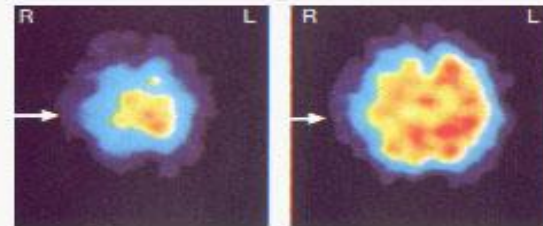
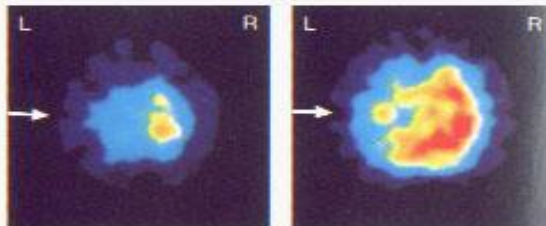
Perfusion defect (stroke) in the right occipital region



Occlusion of the right carotid artery

Pre-operative

Post-operative



Dementia: Pick disease

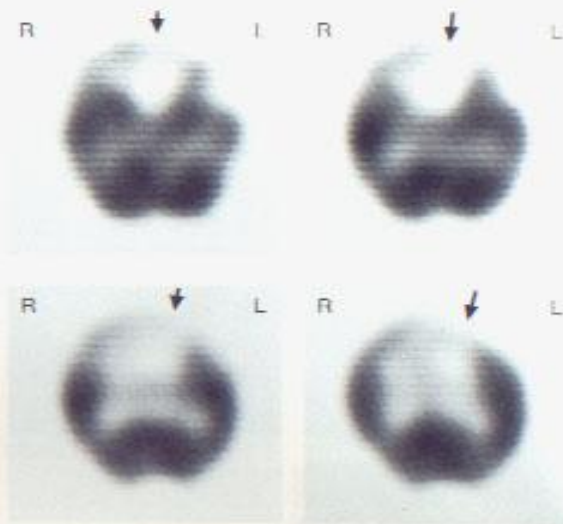
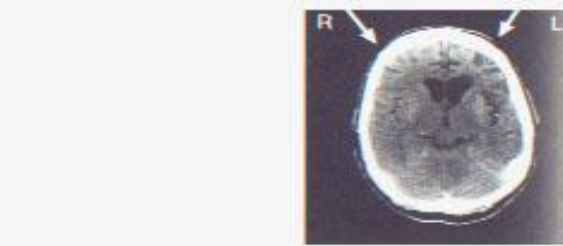


Figure 2a



Figure 2b

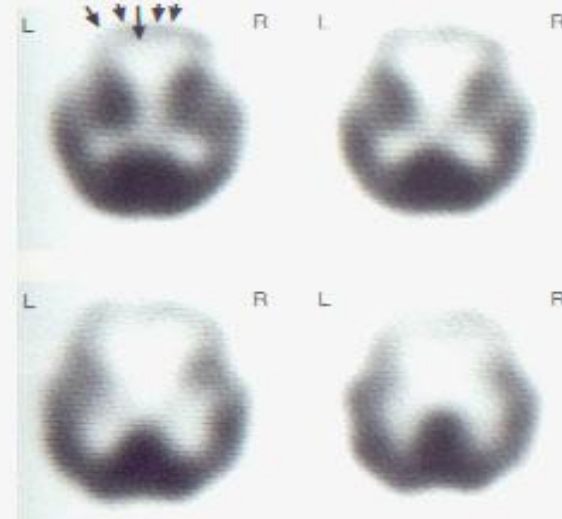


Figure 1a

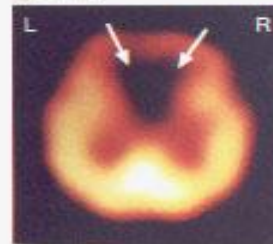


Figure 1b

Hyperperfusion

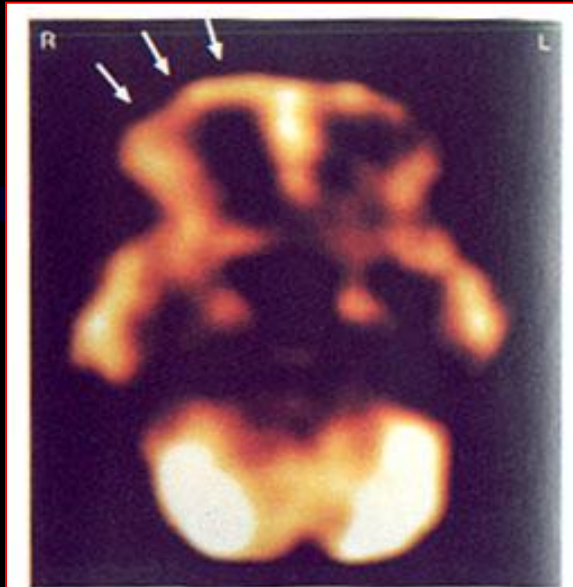


Figure 1



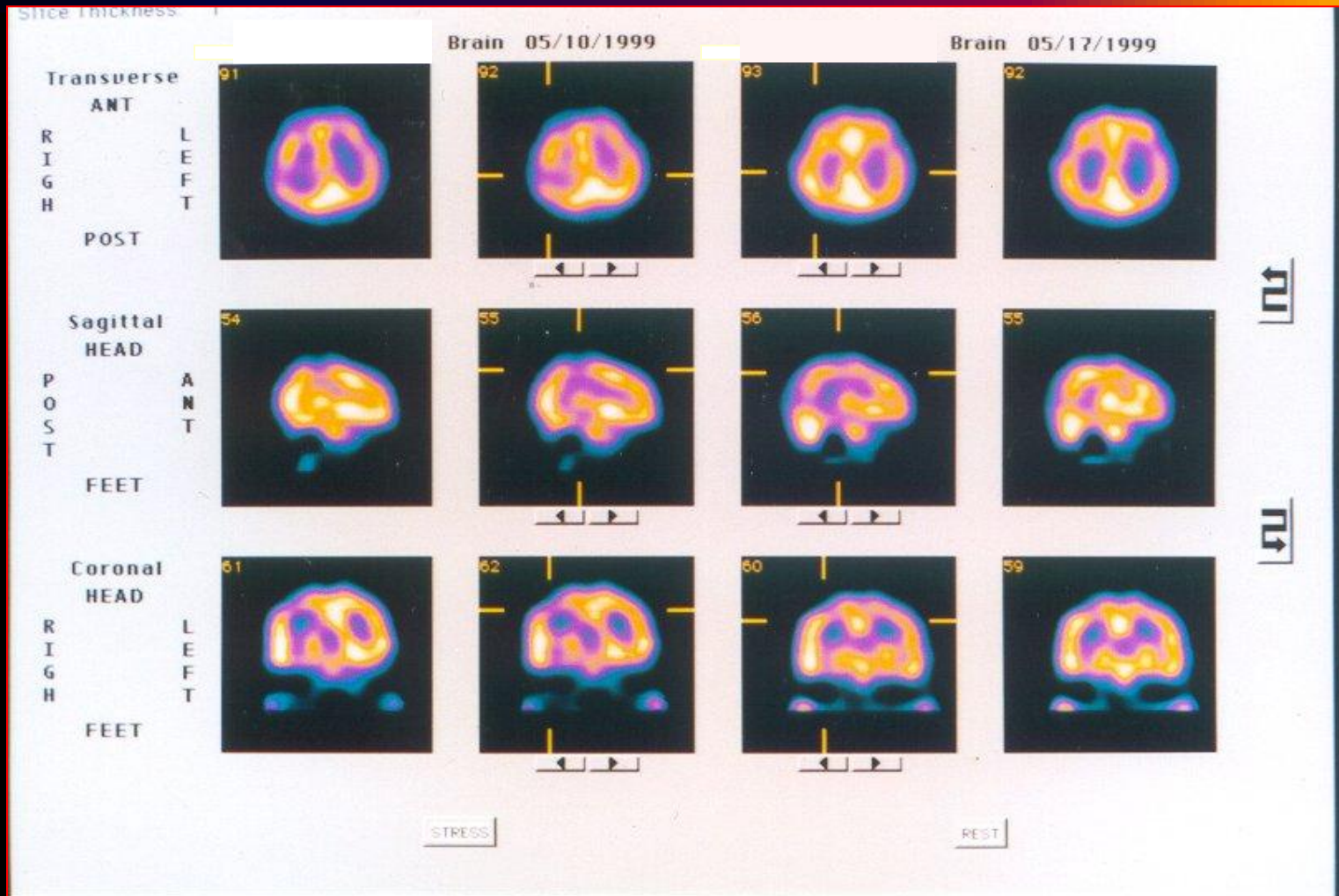
Figure 2

Migraine

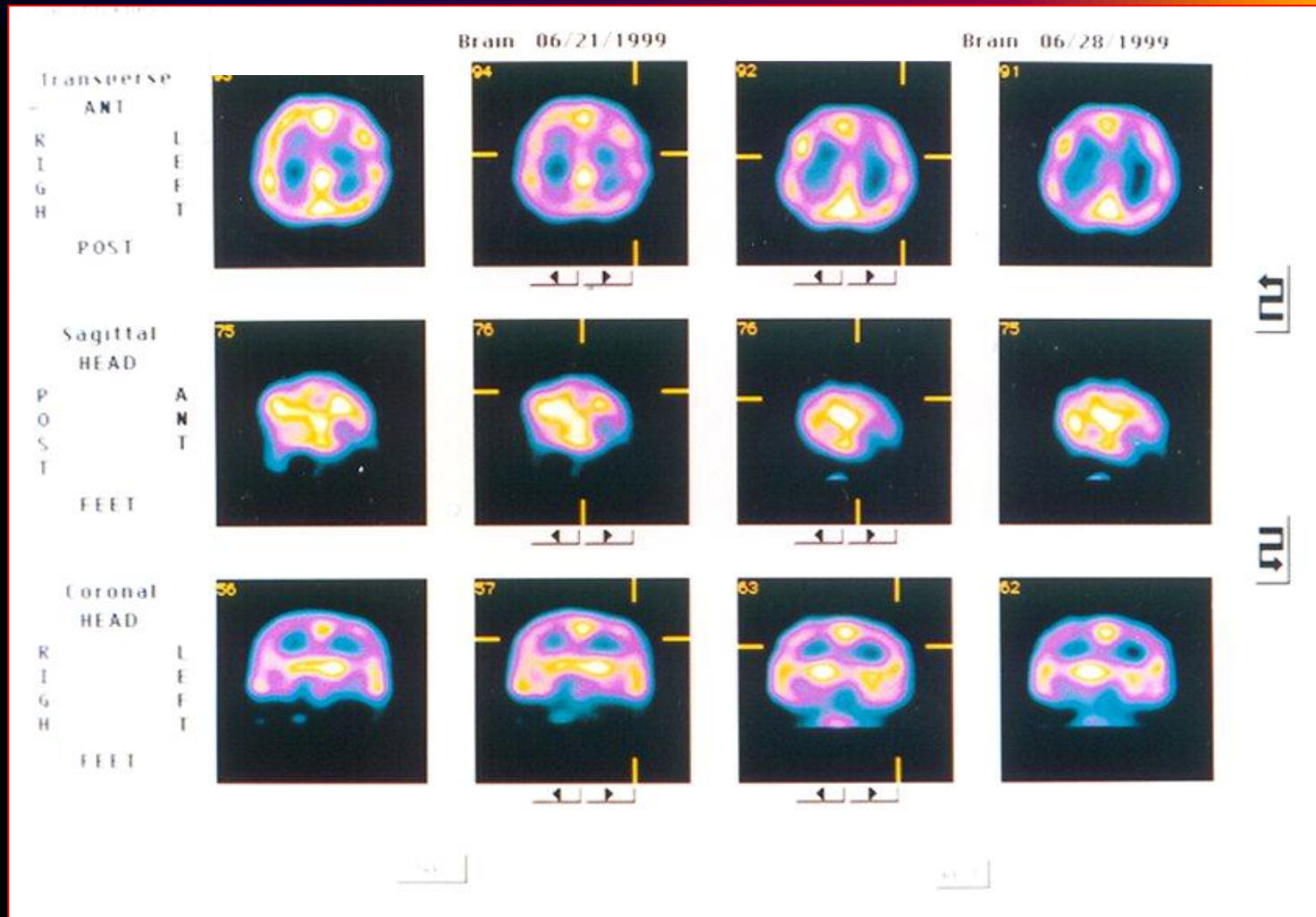
Before treatment

After treatment

51 y., female patient. Complain: numbness of the left arm. Examination: facio-brachial hypalgesia on the left side, accentuated deep tendon reflexes, mild dysmetry, pronation in Barre position (two columns from left: after DP stress)



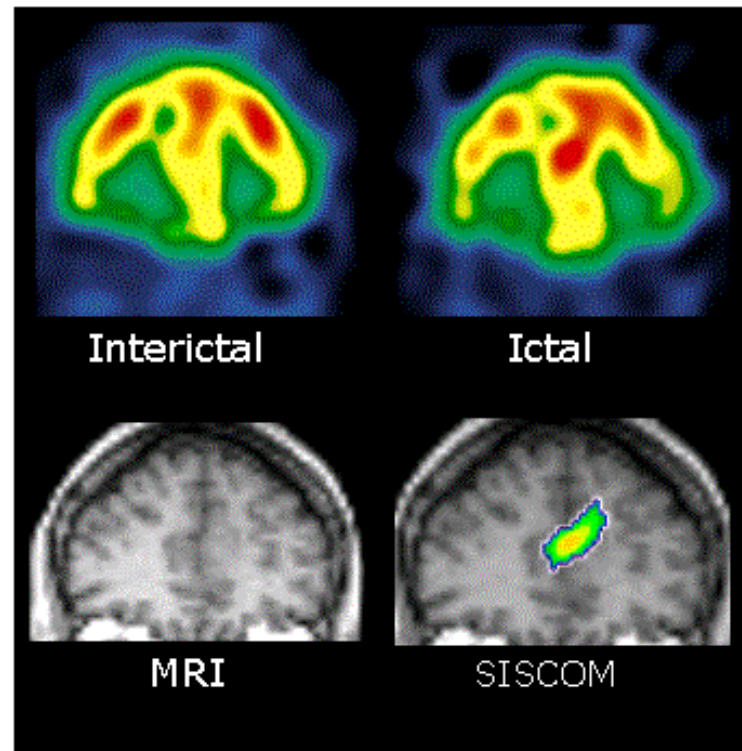
42 y., female patient. Examination: right-sided hemihypalgesia, latent paresis, accentuated deep tendon reflexes, mild dysmetria and dysdiadochokinesis (two column from left: after DP stress)



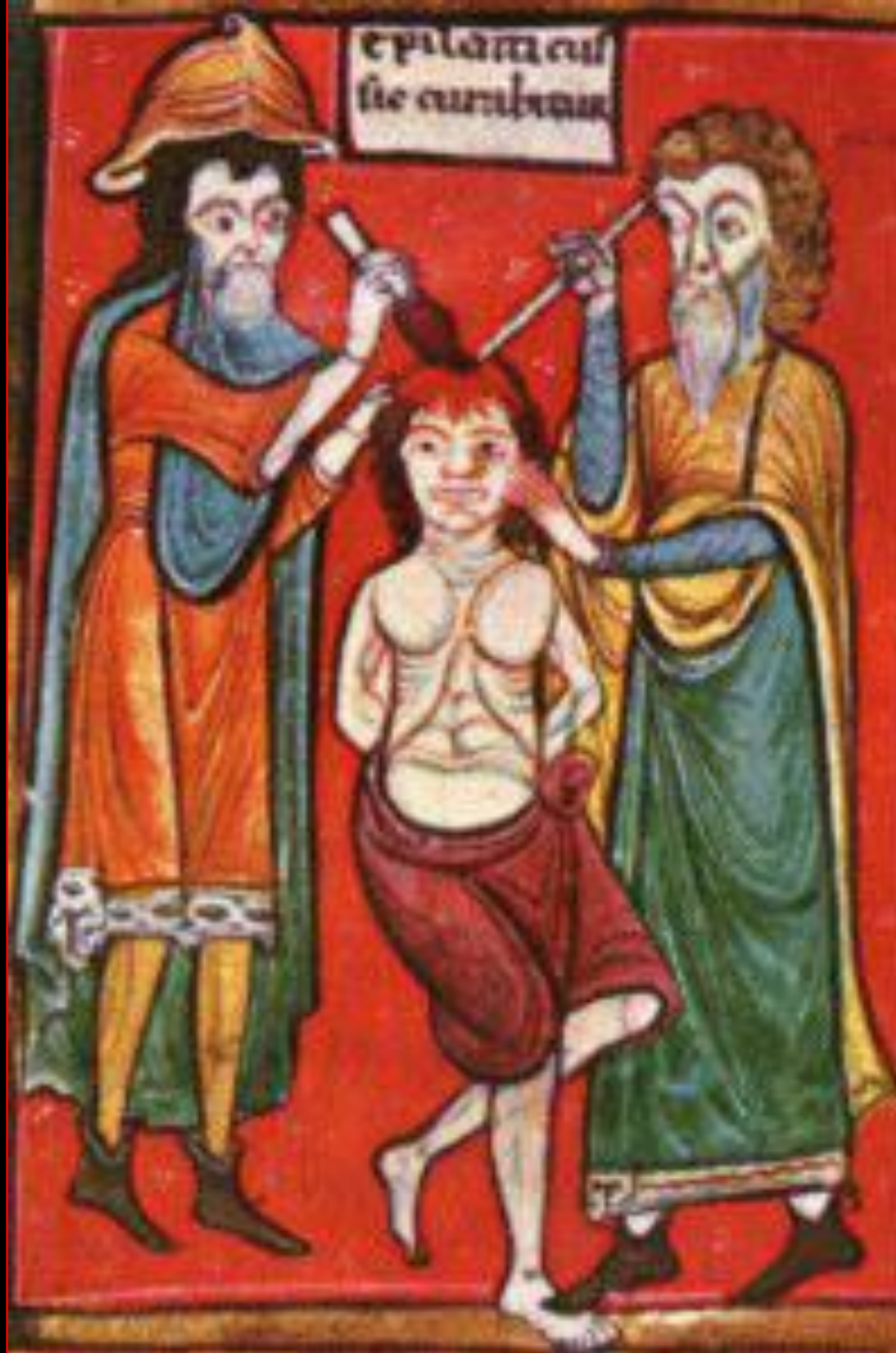
Epilepsy

Methods to process and analyse SPECT images - SISCOM

- Interictal and ictal SPECT images
- Coregistration of interictal and ictal SPECT scans
- Normalisation
- SPECT subtraction
- Thresholding of difference image
- Subtraction SPECT to MRI-coregistration
 - Localization^{1,2}:
 - SISCOM: 88%
 - Side-by-side visual inspection: 39%



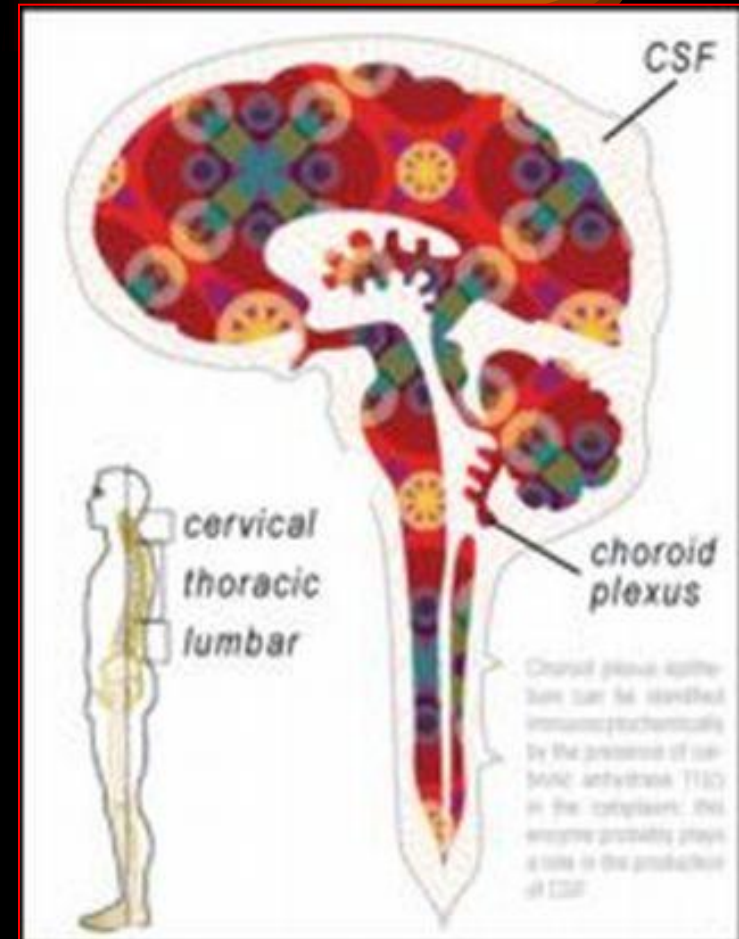
¹O'Brien TJ et al, Neurology 1998; 50: 445-454. ²Lewis PJ et al, J Nucl Med 2000; 41: 1619-1626



Therapy of epilepsy in the XII. Century

Circulation of the cerebrospinal fluid (CSF)

It is produced in the brain by modified ependymal cells in the choroid plexus. It circulates from the choroid plexus through the interventricular foramina (foramen of Monro) into the third ventricle, and then through the mesencephalic duct (cerebral aqueduct) into the fourth ventricle, where it exits through two lateral apertures (foramina of Luschka) and one median aperture (foramen of Magendie). It then flows through the cerebromedullary cistern down the spinal cord and over the cerebral hemispheres.

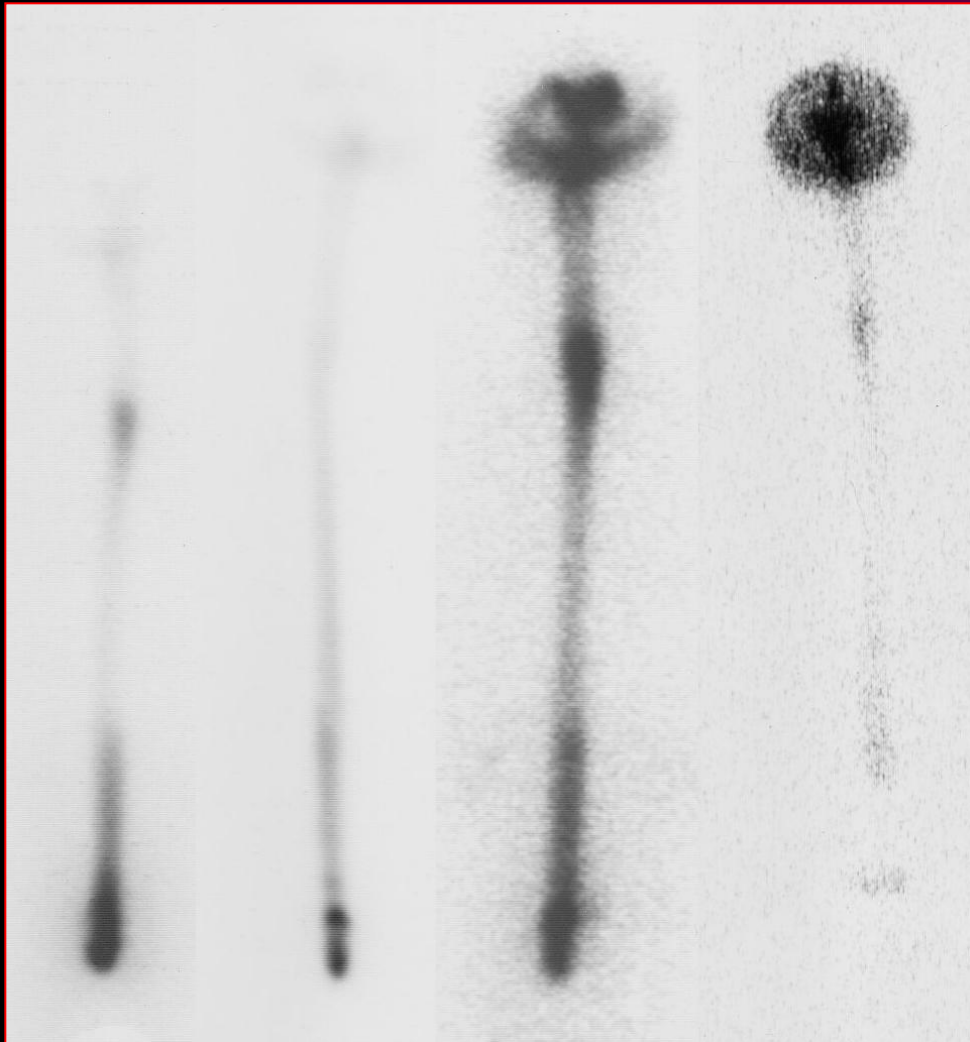


Examination of CSF

- **Radiopharmaceutical:** 500 MBq ^{99m}Tc -DTPA via intrathecal route (lumbar or cisternal)
- Whole body scan + static lateral scans
1, 3, 6, 24 hours after administration
- **Normal dynamic:** cisterna magna-3 hours later, flow to the convexity-6 hours later, predominantly the convexity is shown-24 hours later, no activity in the lateral ventricles!
- **Abnormal:** - slow dynamic (spinal tumor)
- hydrocephalus: reflux – only lateral ventricles

Liquor dynamic investigation in a patient with reflux (lumbar administration)

1 hour 3 hrs 6 hrs 24 hrs



right left

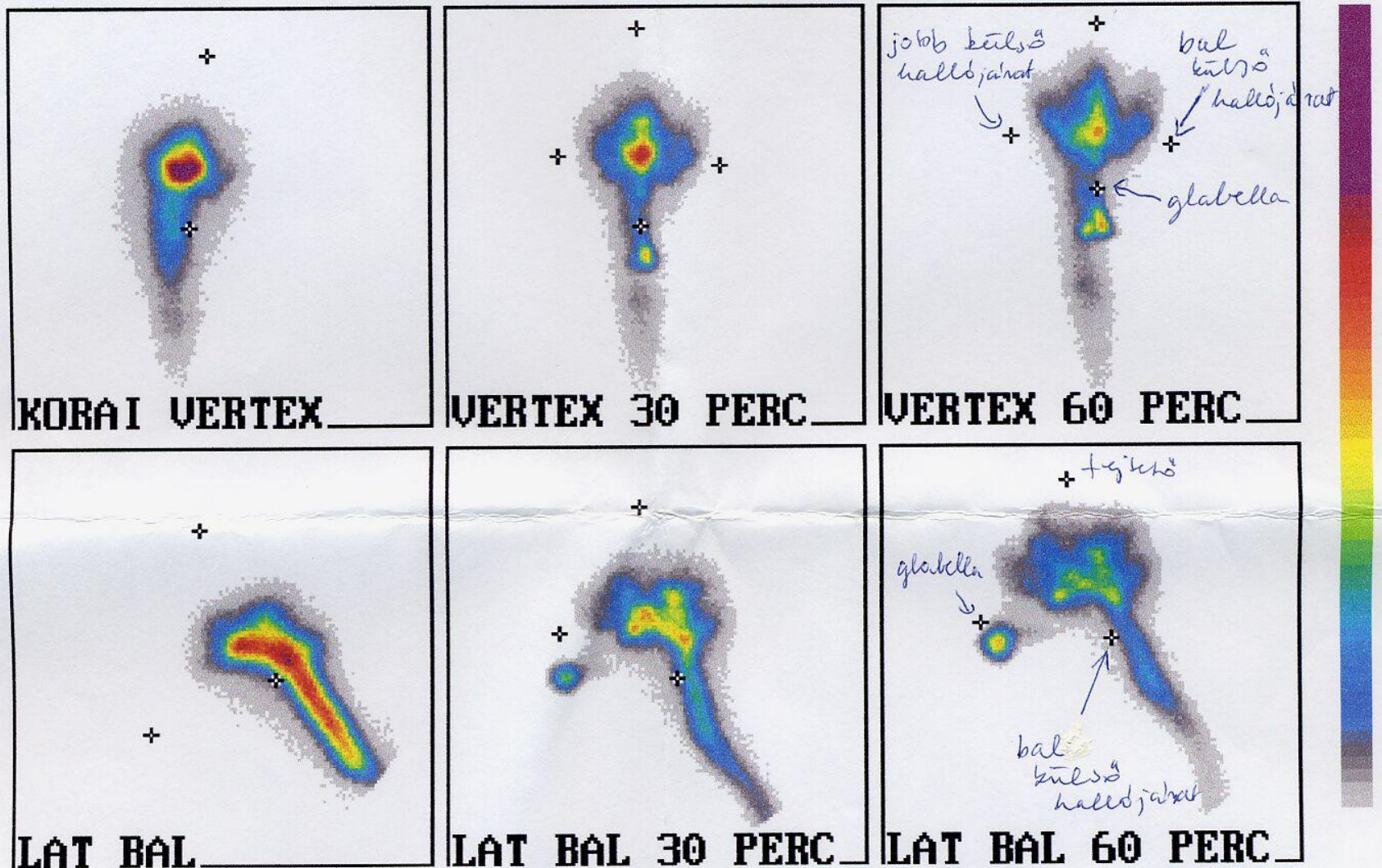


3 hrs

6 hrs

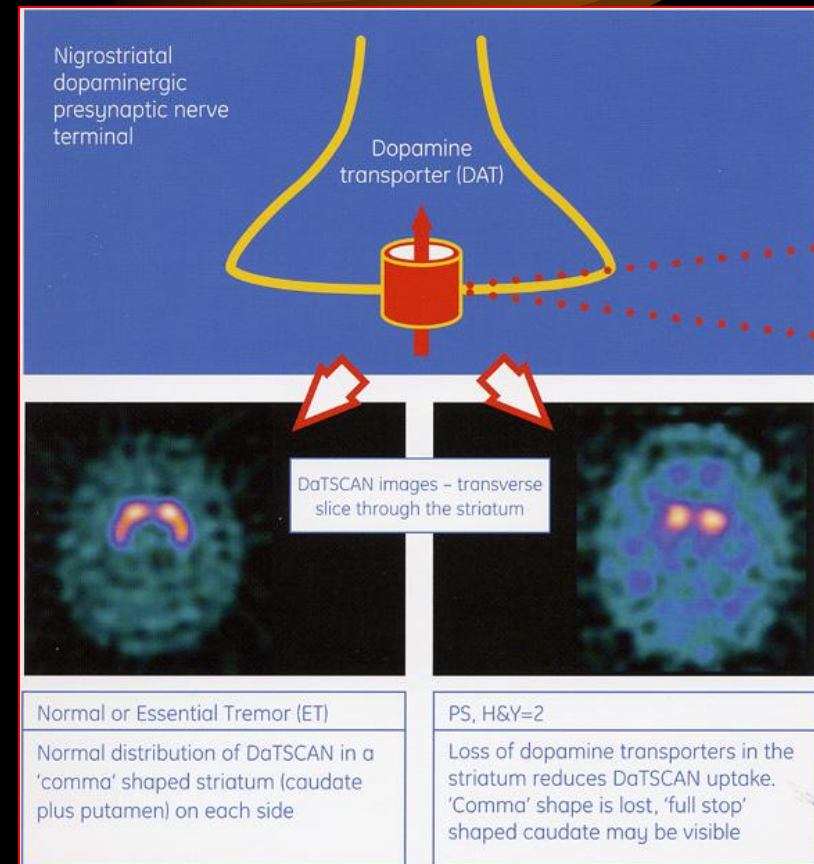
24 hrs

Investigation of liquorrohea (cisternal administration)



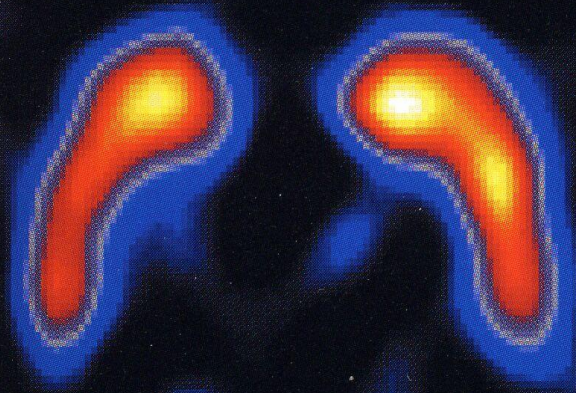
Theory of presynaptic dopamine receptor scintigraphy

- DATSCAN™ binds to the **dopamine transporters (DAT)**, which are on the neurons in specific areas of the brain. When neuronal degeneration is present, the number of DAT are **significantly reduced** (for example in patients with **Parkinson's disease**).
- By detecting the binding of DATSCAN™ to the dopamine transporters will be a clear visualisation of dopamine transporter integrity and consequently an **accurate diagnosis** of disease.

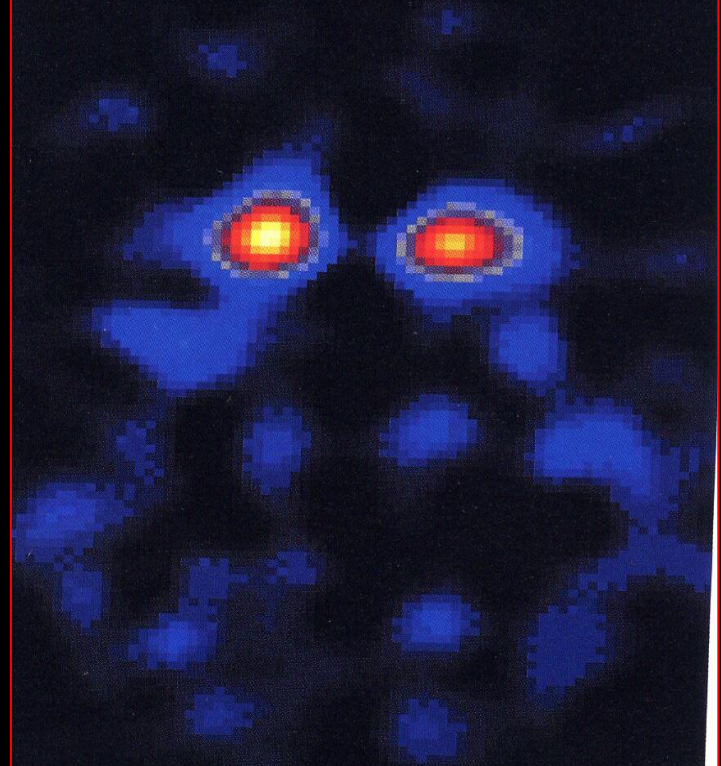


Dopamin receptor examination (DATSCAN™) in a patient with Parkinson's disease

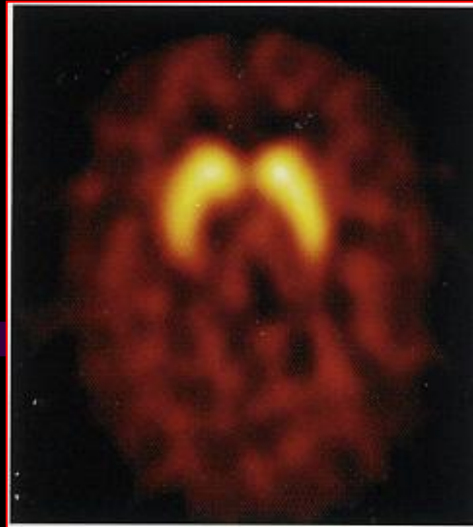
Normal distribution



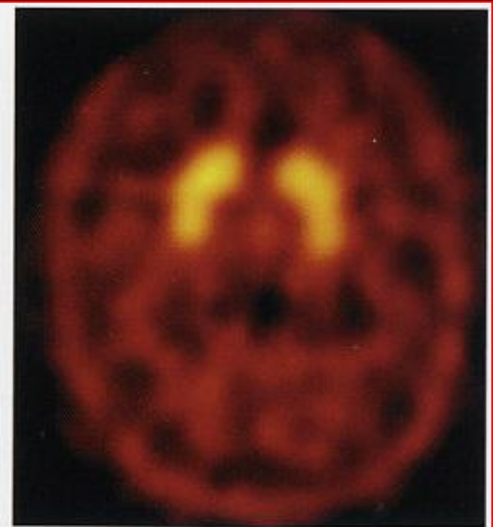
Absence of receptors



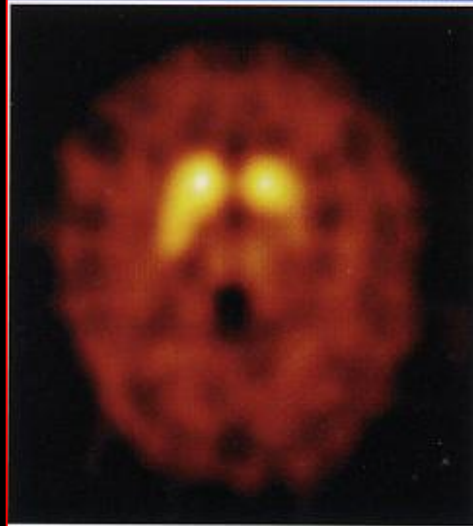
Presynaptic dopamin receptor examination in different disorders



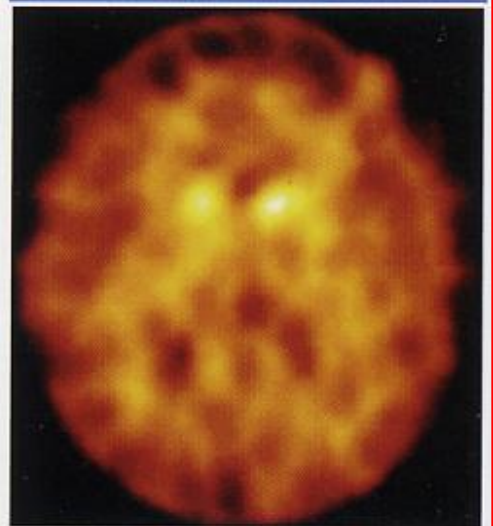
Healthy control



ET



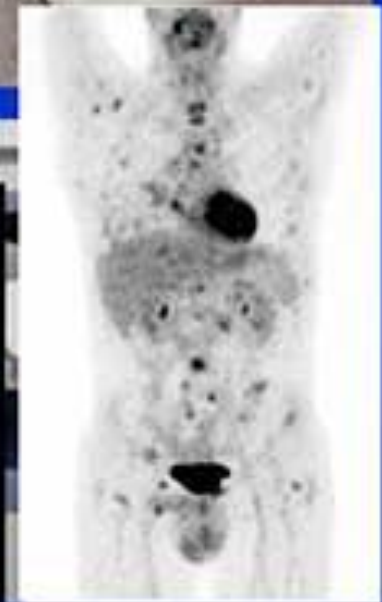
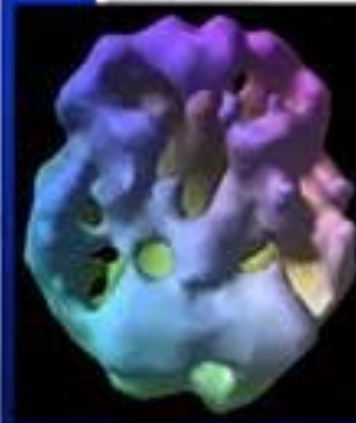
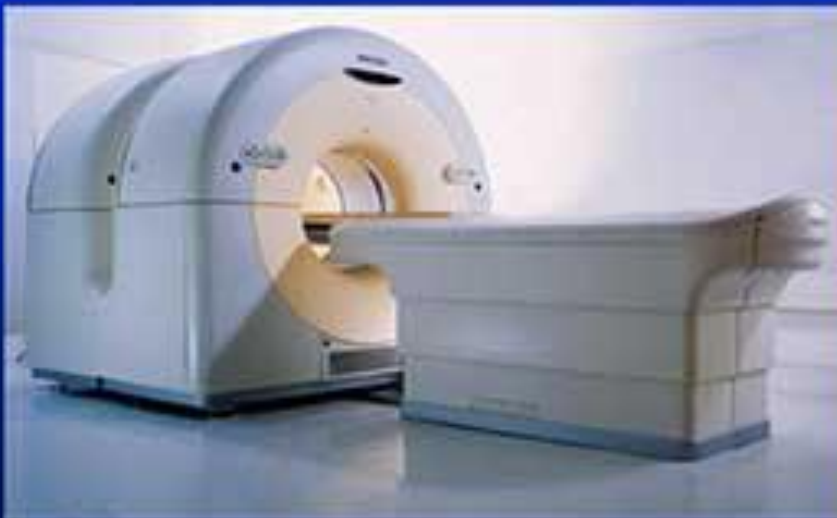
Early stage PD, H&Y=1



Advanced stage PD,
H&Y=4

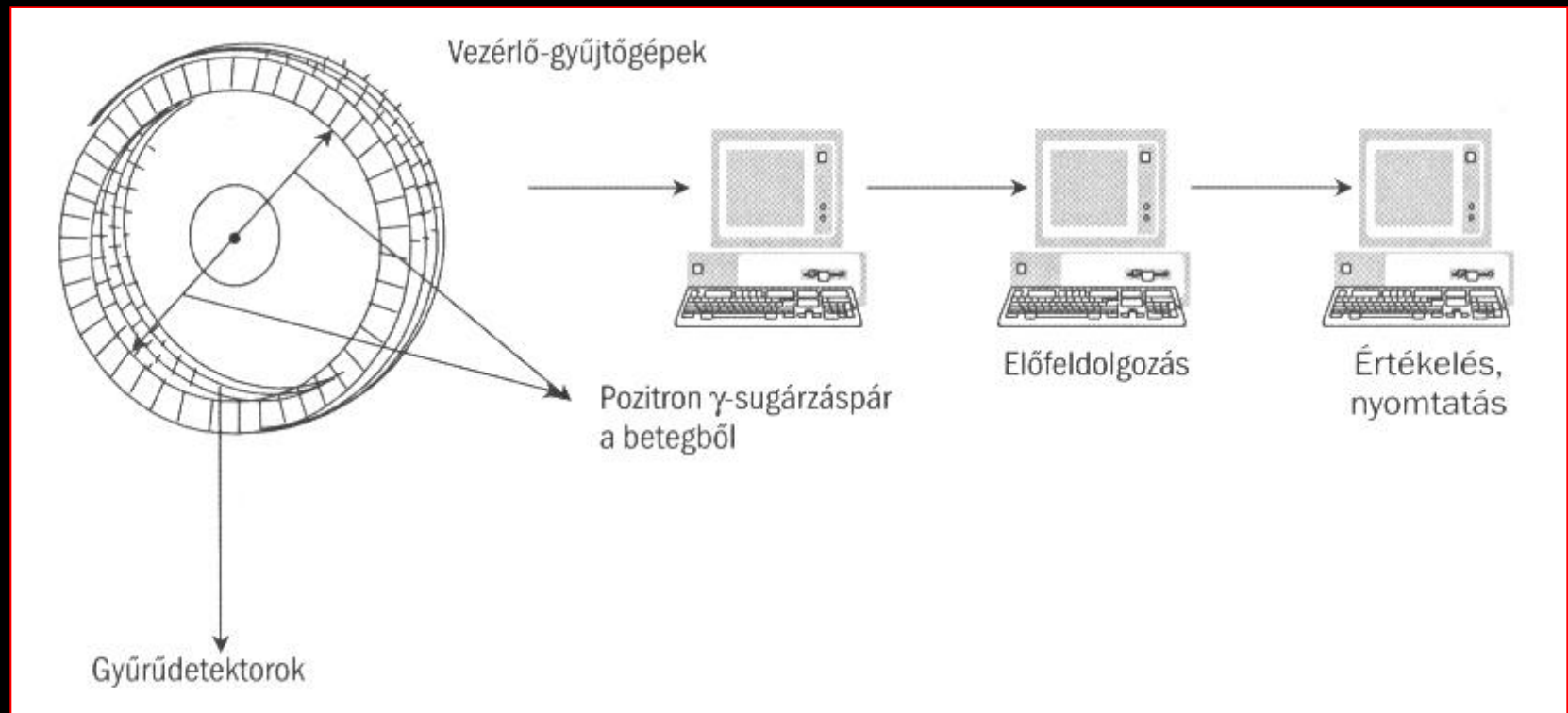
PET/CT (positron emission tomograph)

This is the „today's" method

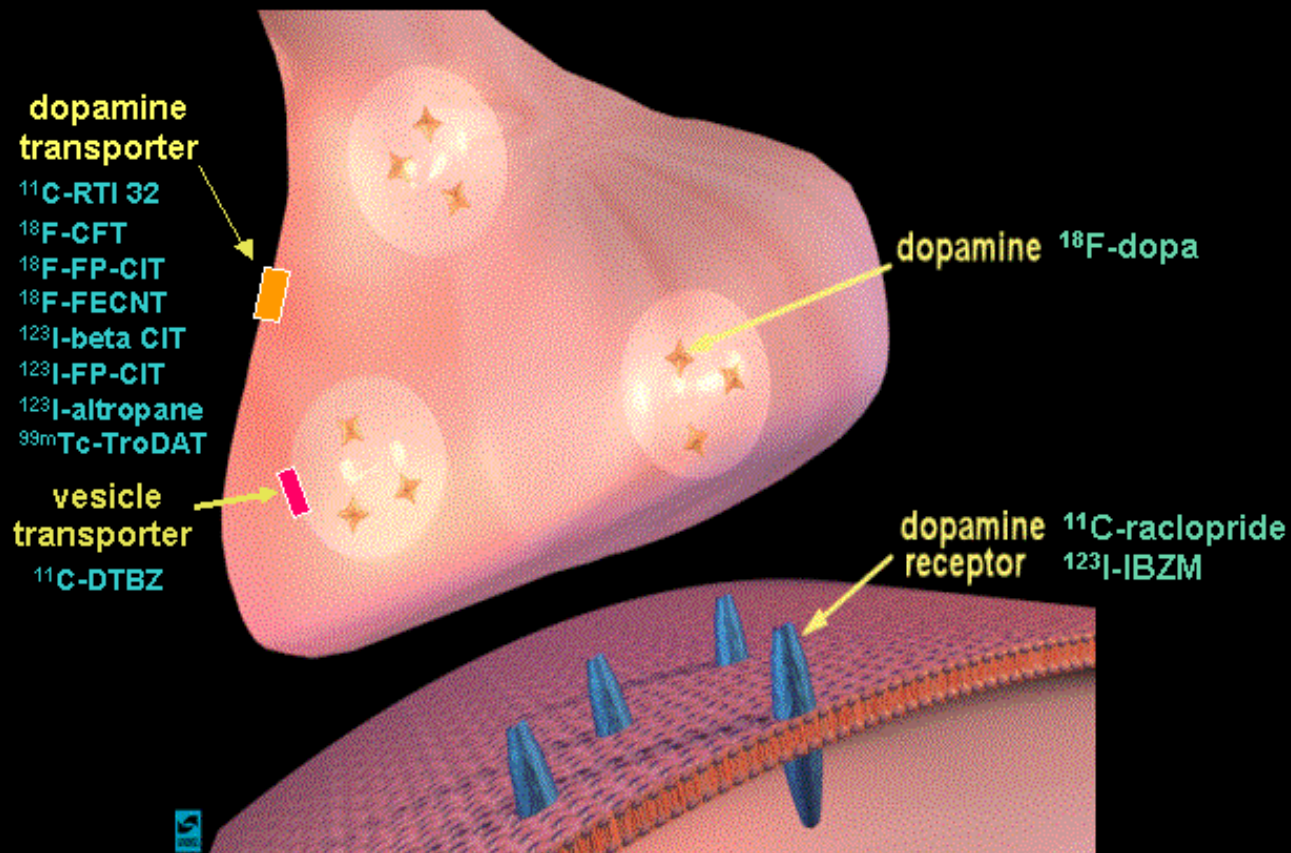


How the PET works:

- The injected radiopharmaceutical is a **positron emitted** substance, the equipment is capable to detect the annihilation-rays (**two gamma-photons with 511 keV**)
- Usage of isotopes with ultrashort half-life (^{11}C , ^{15}O , ^{13}N , ^{18}F), which are suitable for measurement of metabolic processes



Neuroreceptor studies



^{11}C -RTI 32

^{123}I -FP-CIT

^{11}C -DTBZ

^{18}F -dopa

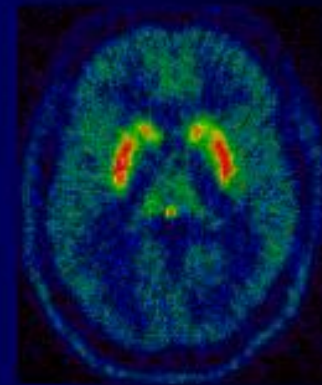
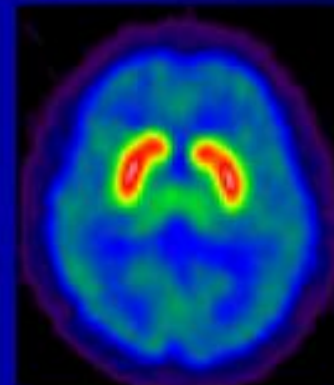
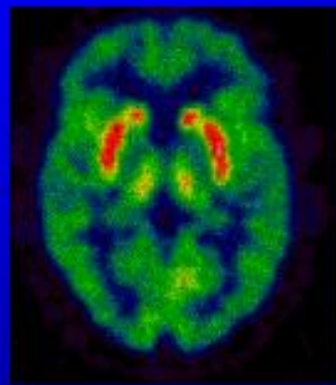
DAT

DAT

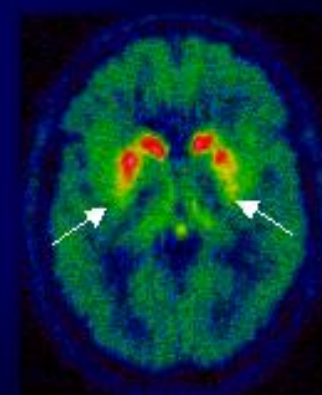
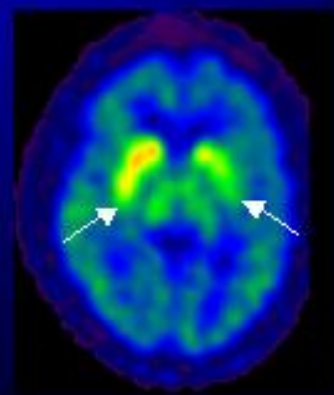
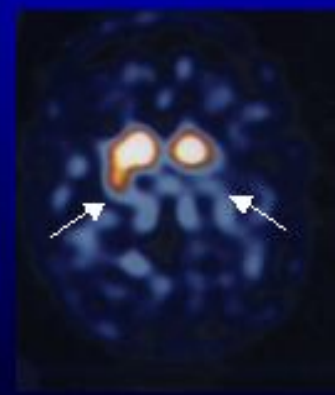
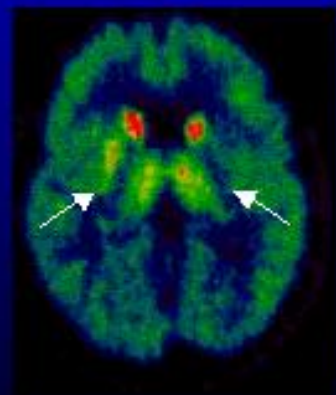
VMAT2

DDC

Healthy

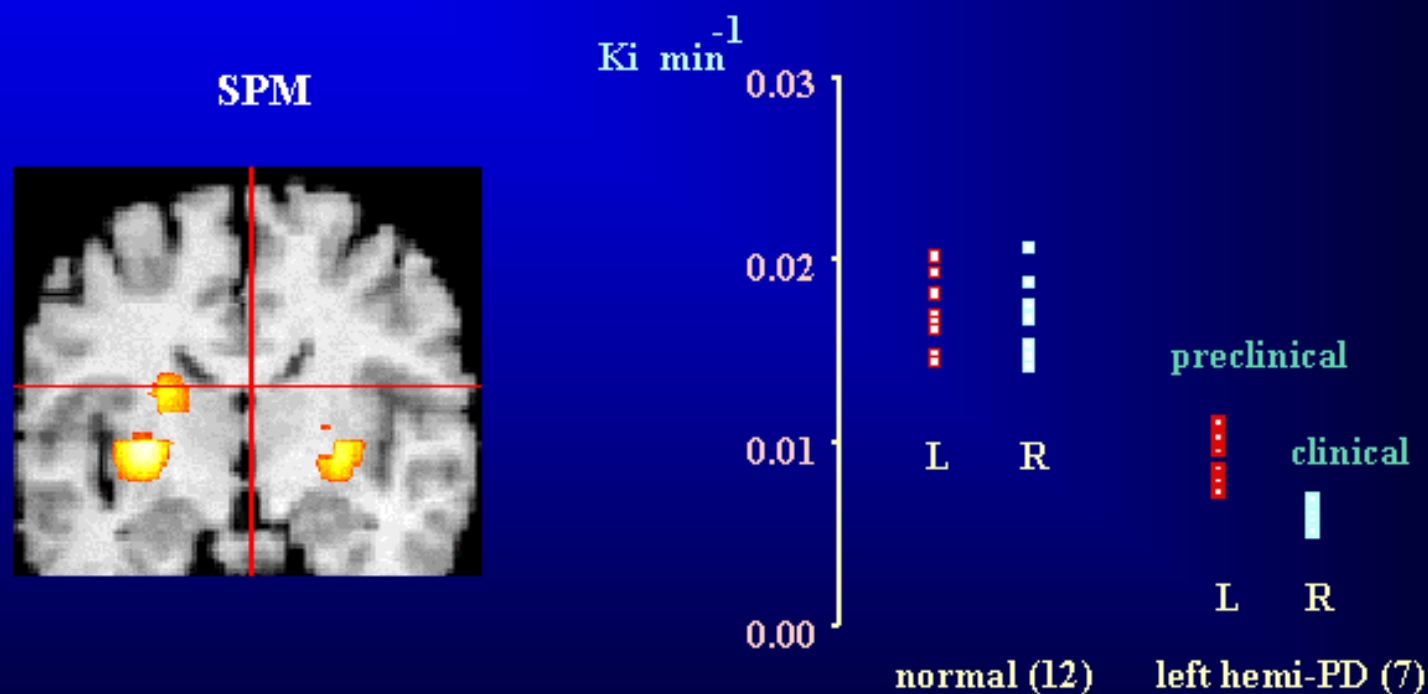


PD



¹⁸F-dopa PET

Putamen uptake in early hemi-PD



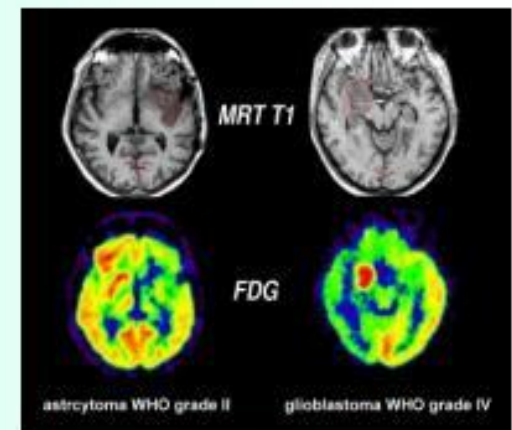
Indications of PET/CT

- **Differential diagnosis of Parkinson's disease**
- **Dementia**
- **Tumors**
- **Presurgical localization of epileptic foci**
- **Therapy monitoring**
- **Neuroreceptor imaging**
- **Task-related mapping of the human cortex**



Is it a malignant tumour

- **FDG uptake is related to histological tumor grade** (Di Chiro et al. 1982; Alavi et al. 1988)
- **FDG uptake in low-grade gliomas** is usually close to that of normal white matter,
- **grade 3 gliomas** have FDG uptake similar to or even exceeding that of normal grey matter.
- **glioblastomas** usually also show high uptake, which may be inhomogeneous due to microscopic and macroscopic necroses that are typical for this tumor type





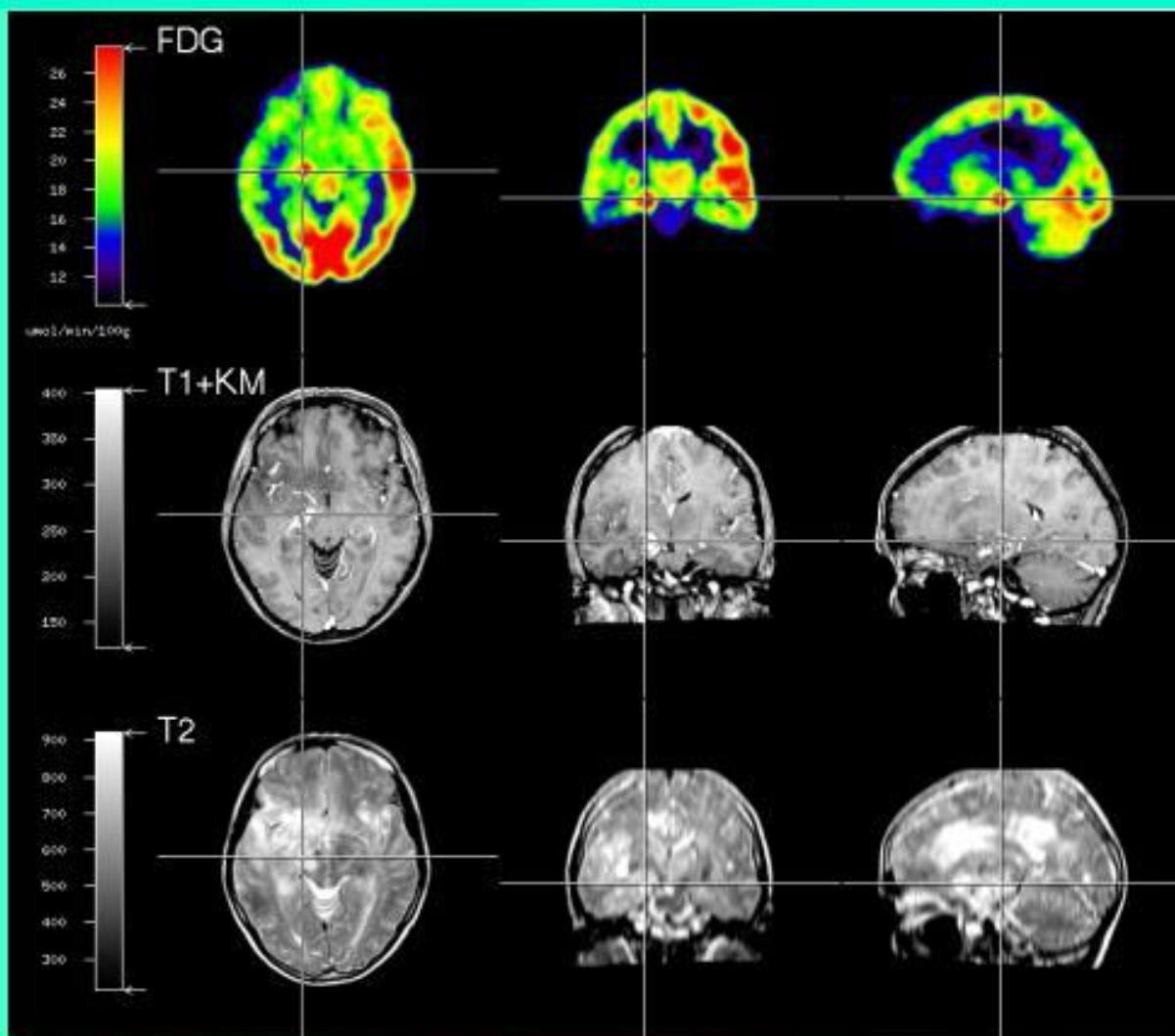
Target for biopsy ?

Stereotactic biopsy offers a possibility to obtain a histological diagnosis in lesions of unknown dignity but may sample material that does not represent the most malignant part of the tumor (Jackson et al. 2001)

It has been demonstrated that the most metabolically active tumor part on **FDG-PET indicates the most informative location for taking a biopsy** (Levivier et al. 1995)



Target for biopsy ?

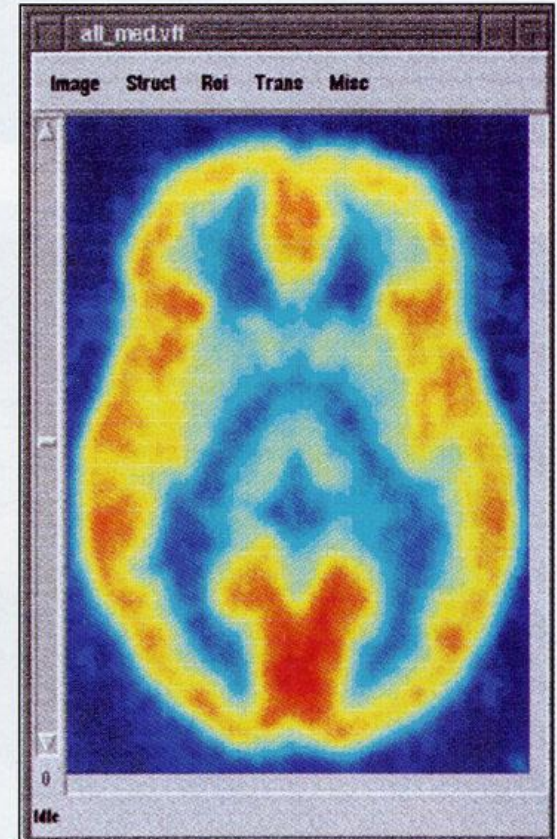
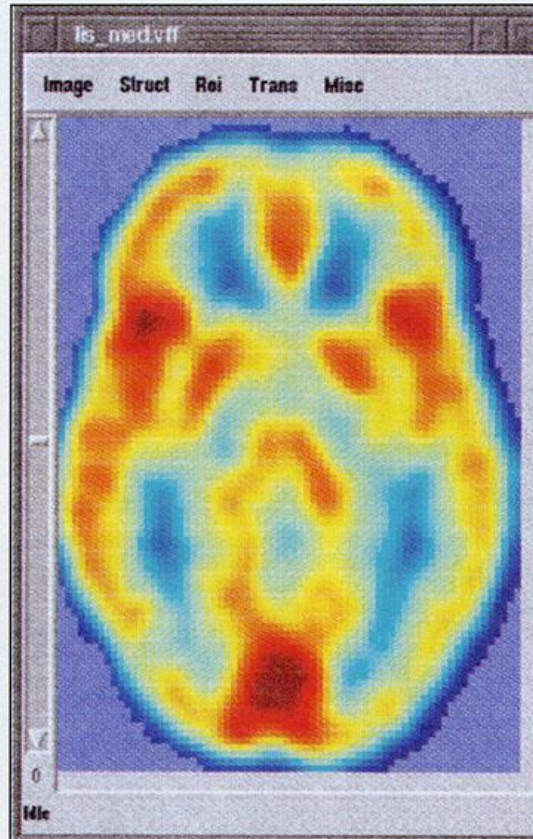
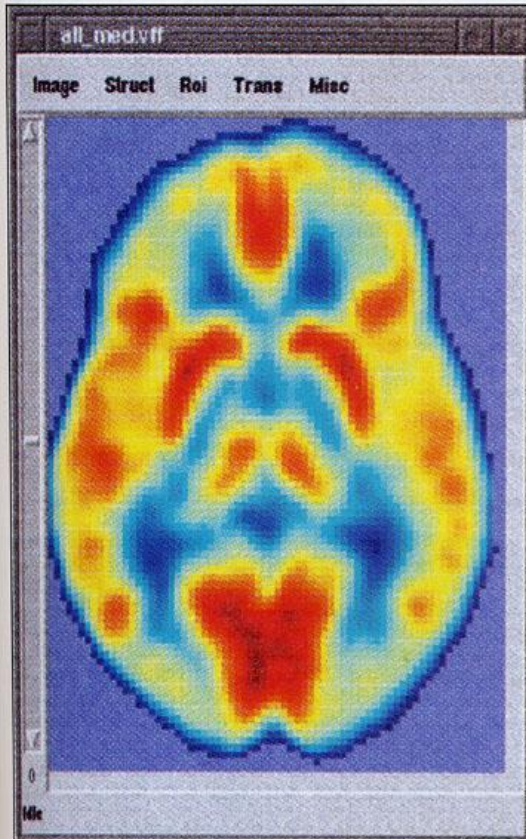


Brain PET with different ligands (normal uptake and distribution)

^{18}F -FDG

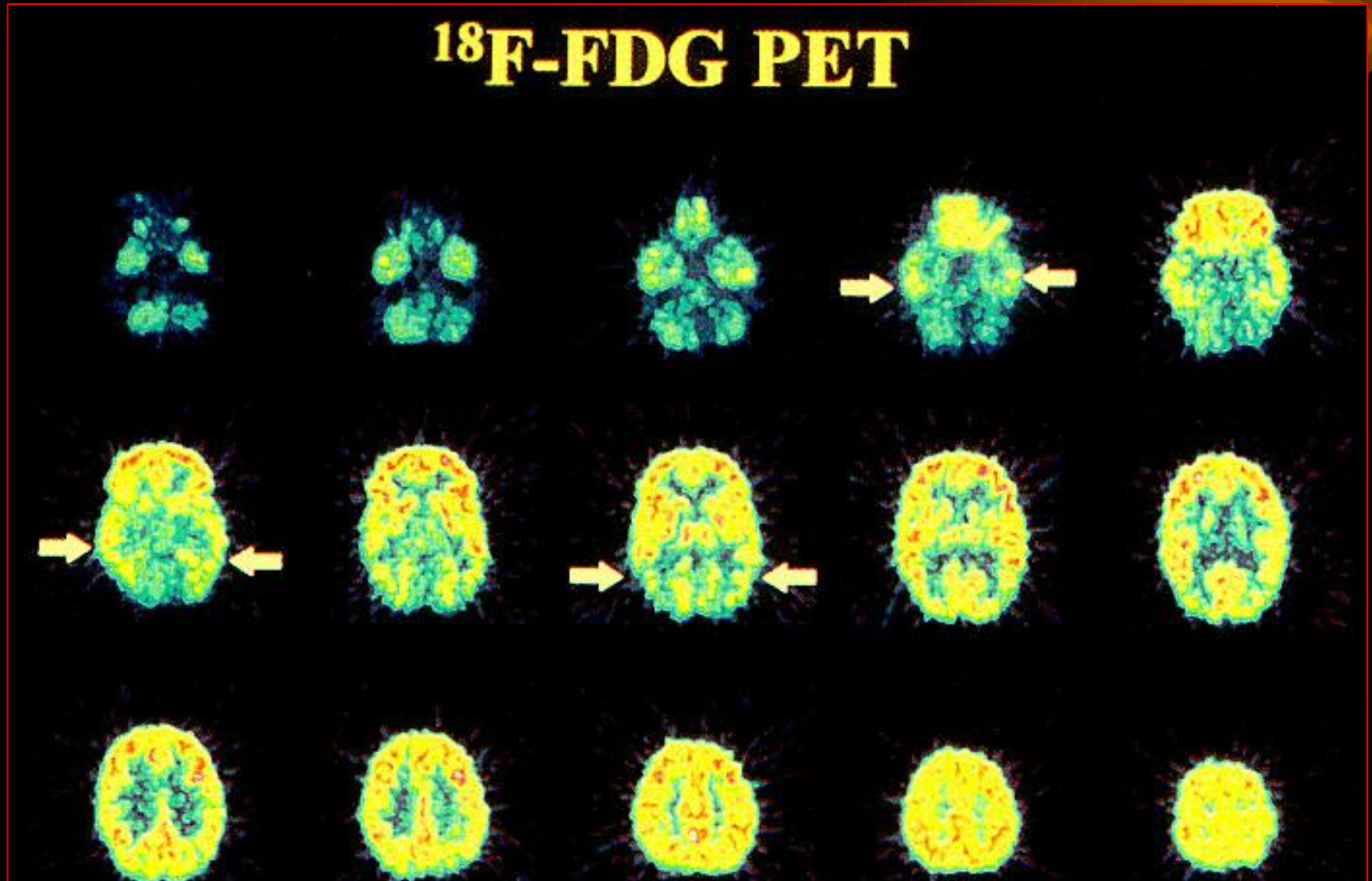
^{15}O -butanol

^{11}C -flumazenil



Alzheimer disease: decreased bilateral temporal glucose metabolism

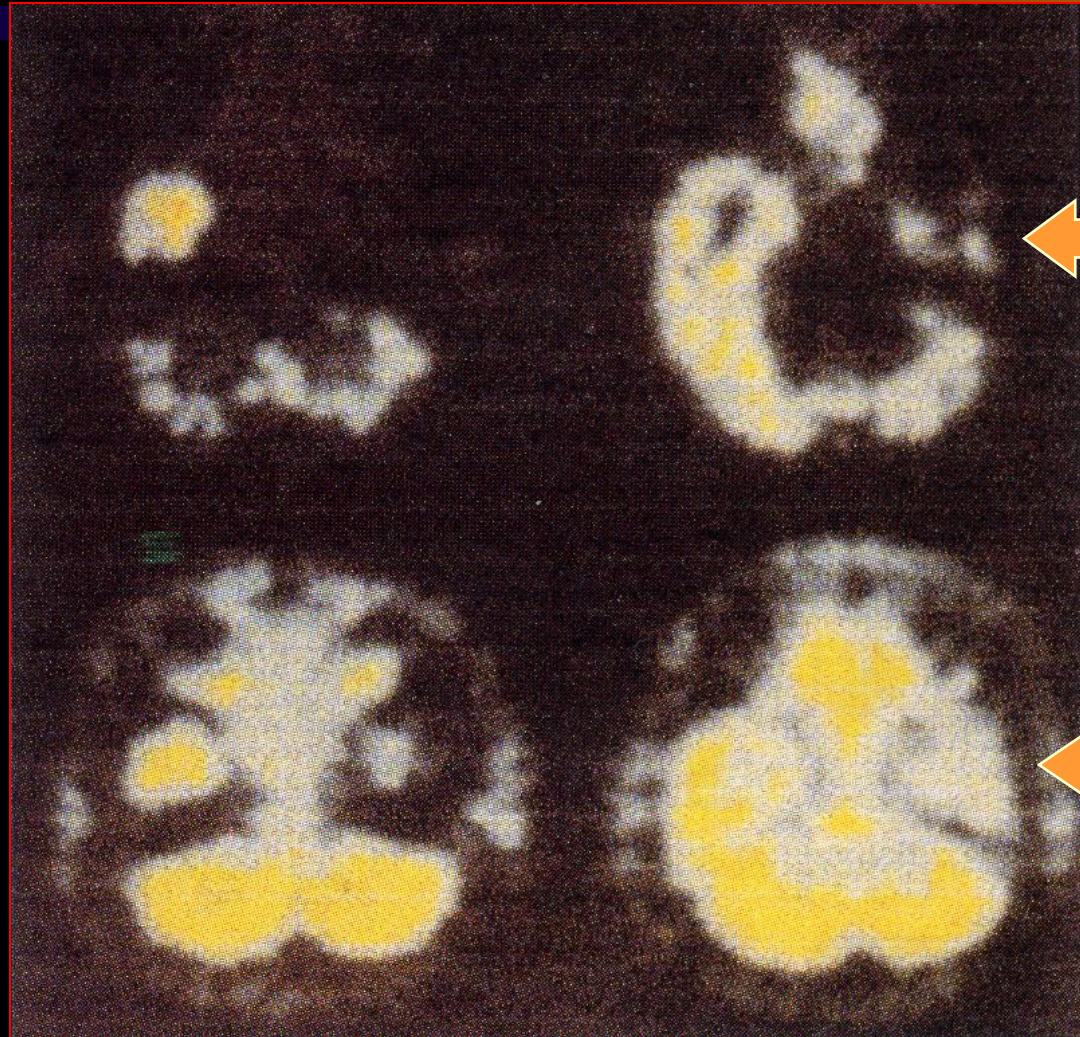
^{18}F -FDG PET



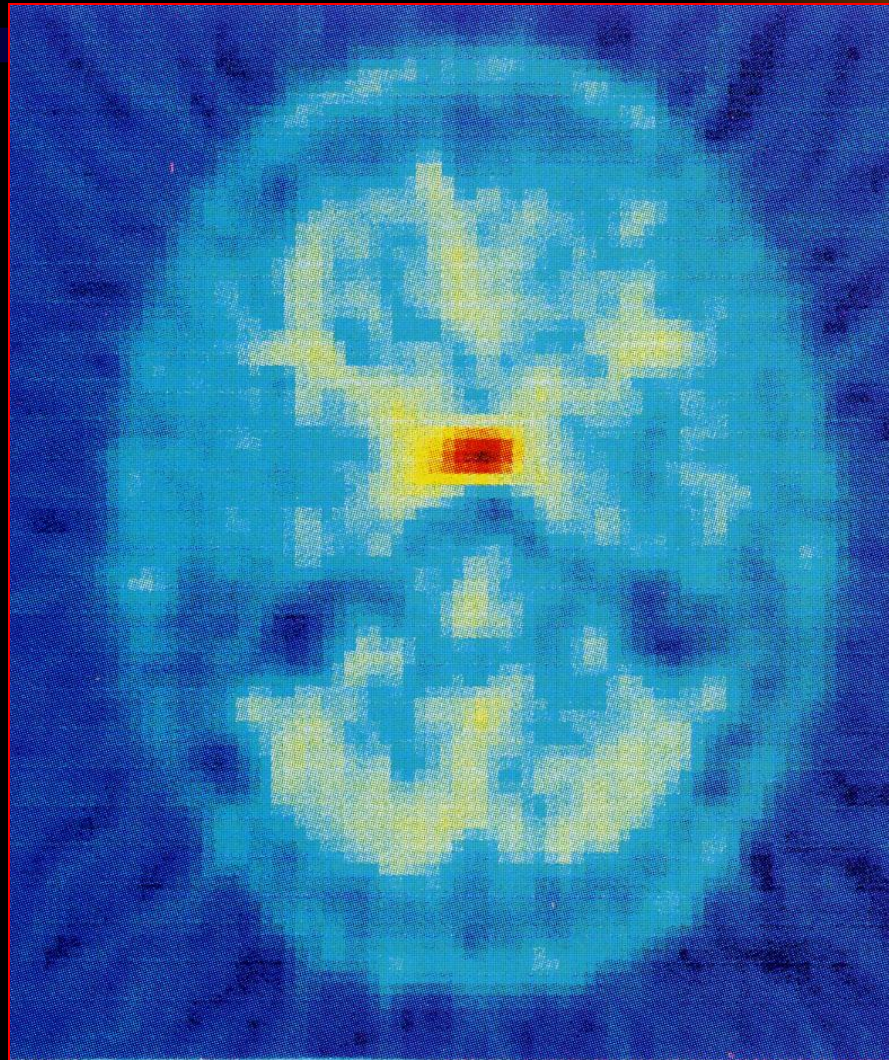
Epileptic focus: decreased activity

^{11}C -flumazenil

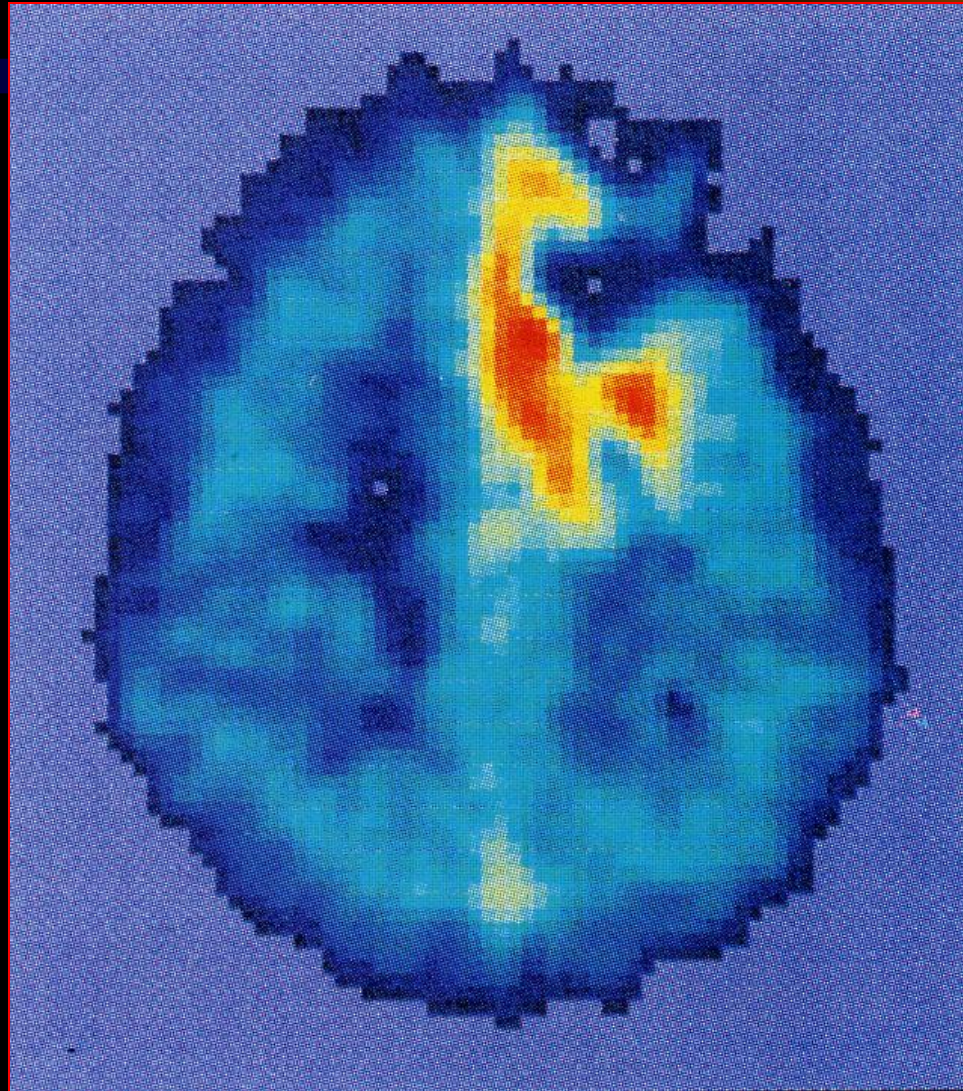
^{18}F -FDG



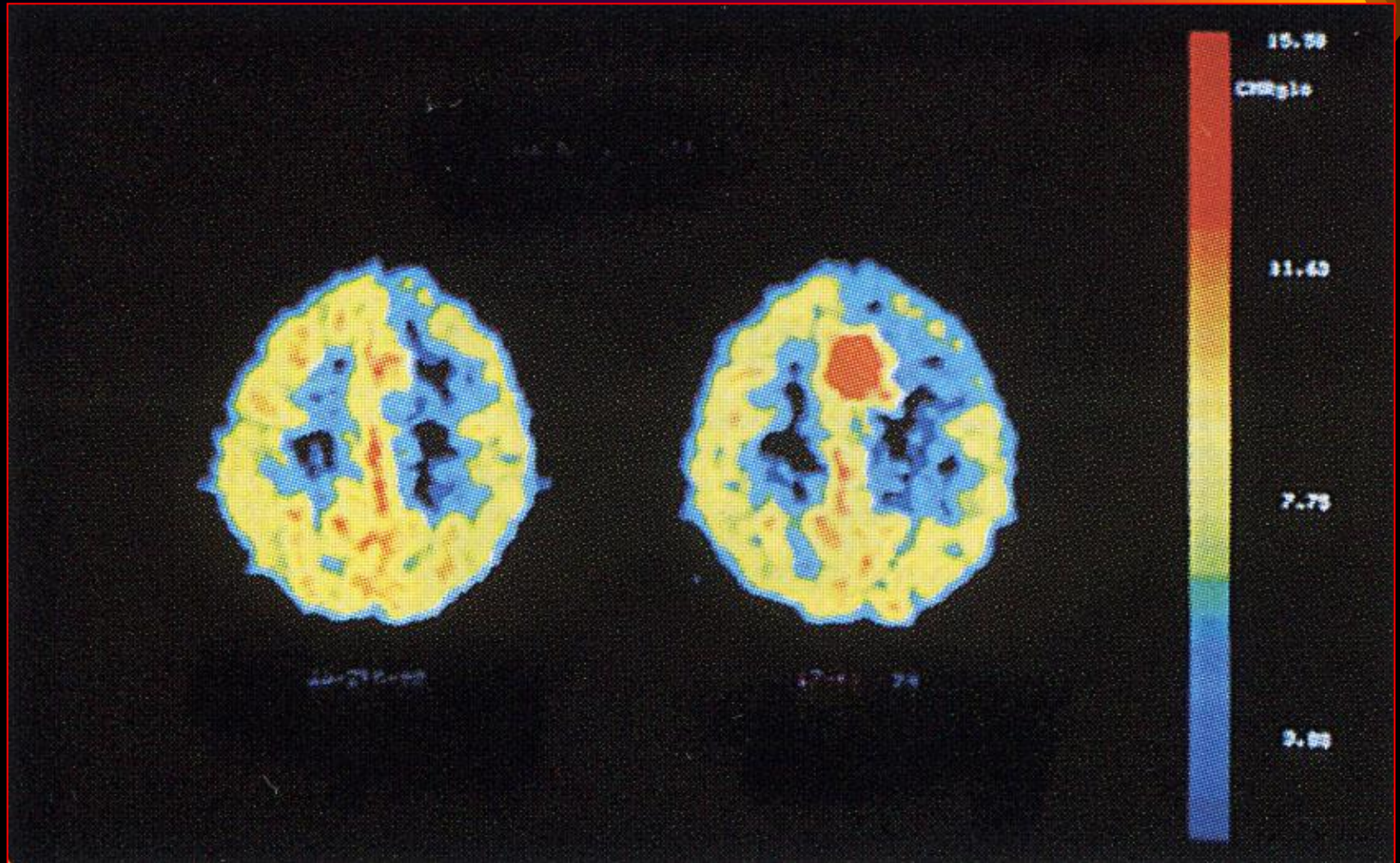
^{11}C -metionin uptake: microadenoma



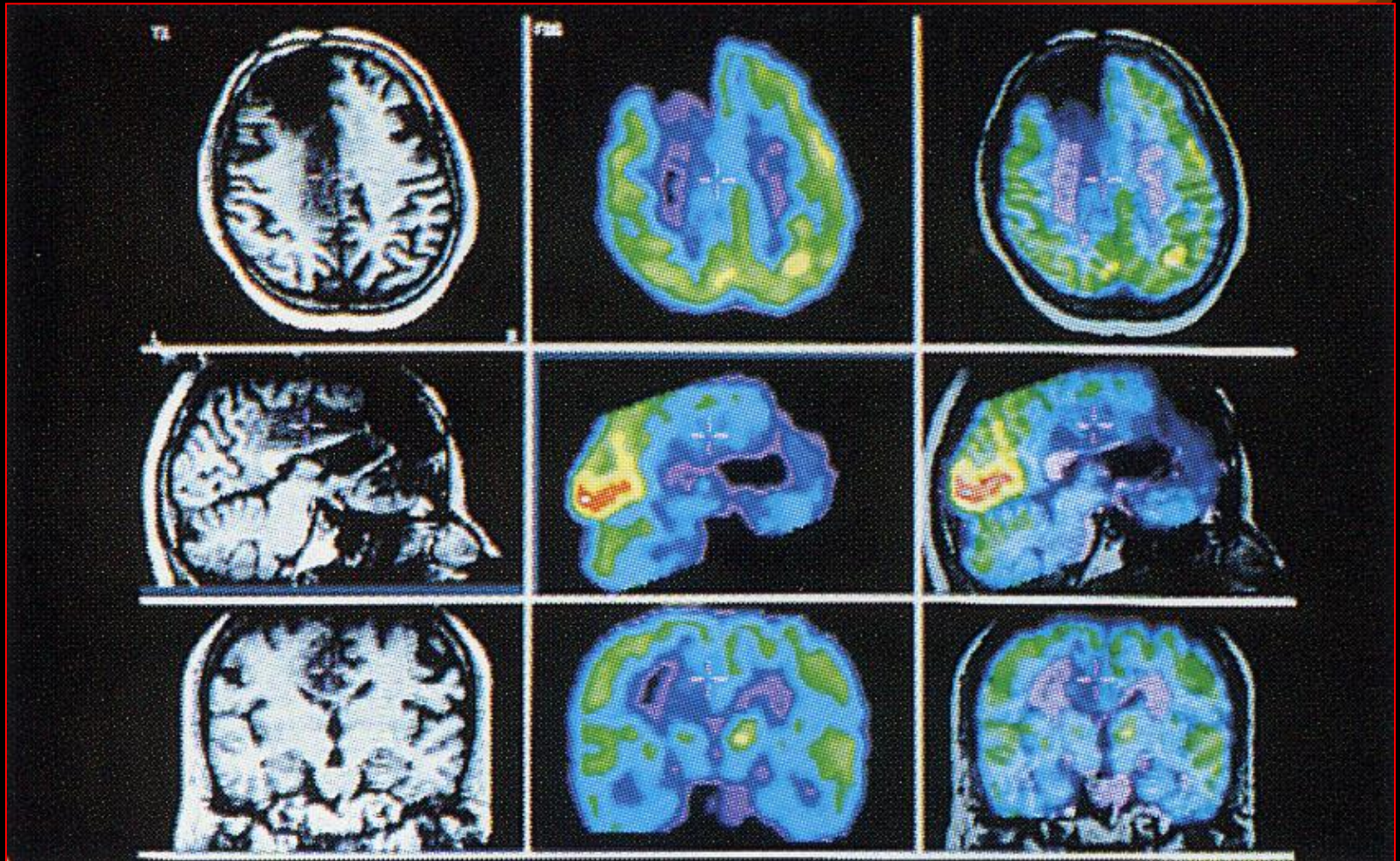
^{18}F -FDG uptake after surgery of a recurrent tumor



Revealing of recurrence of a parasagittal meningioma by ^{18}F -FDG



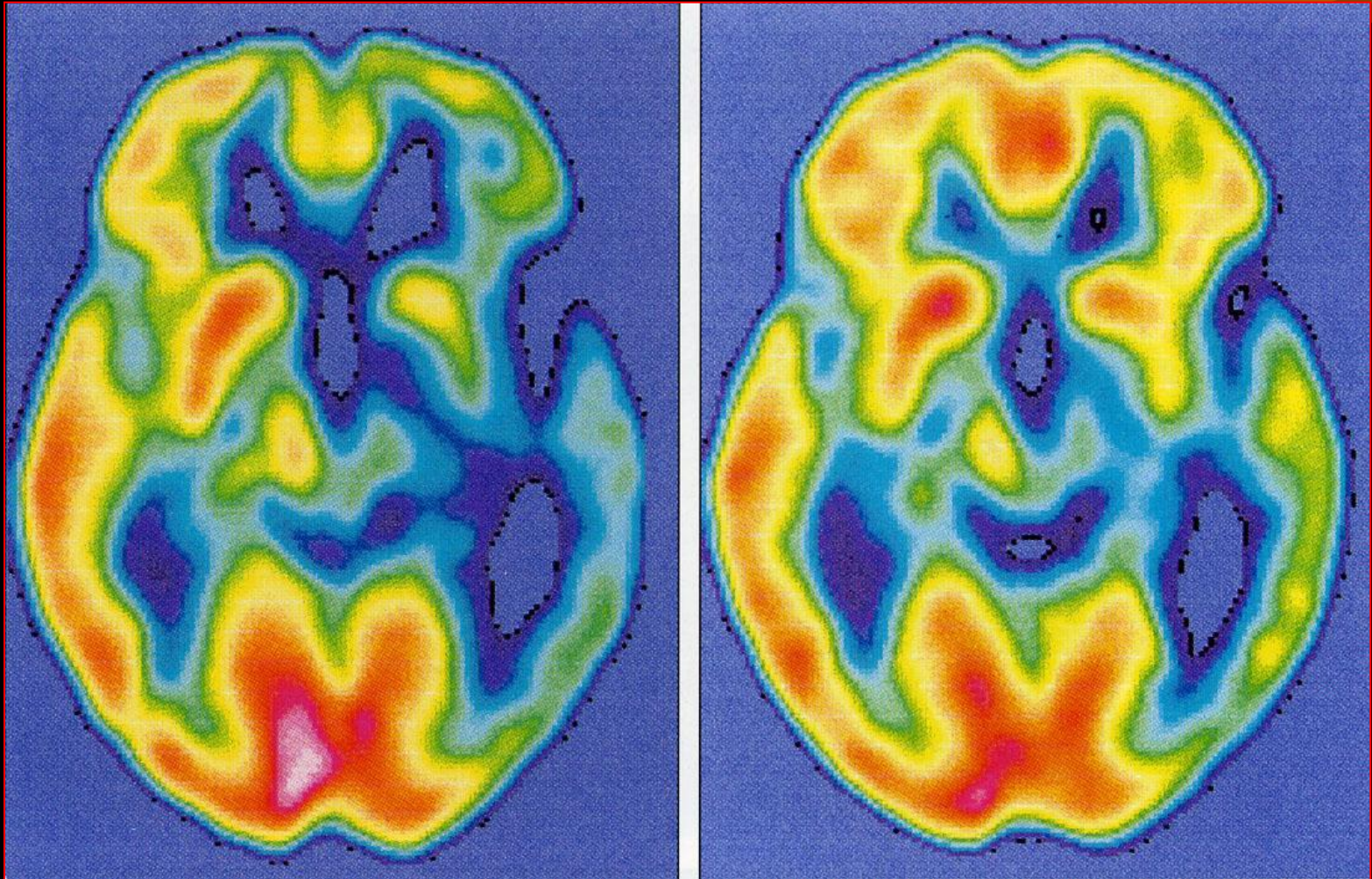
18F-FDG PET-MR fused scan of a glioma's recurrence after surgery



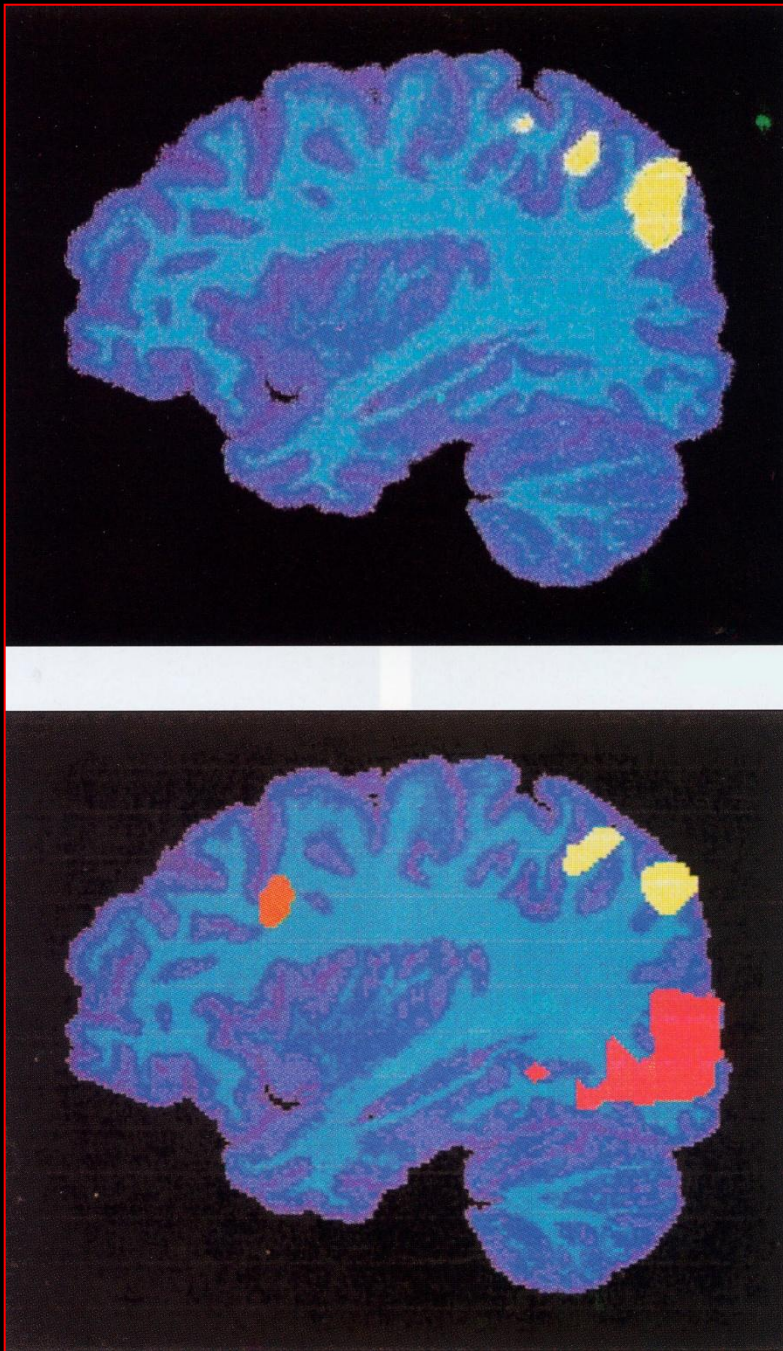
Evaluation of therapeutic effects by ^{18}F -FDG

Stroke

after vinpocetin infusion
(2 weeks later)

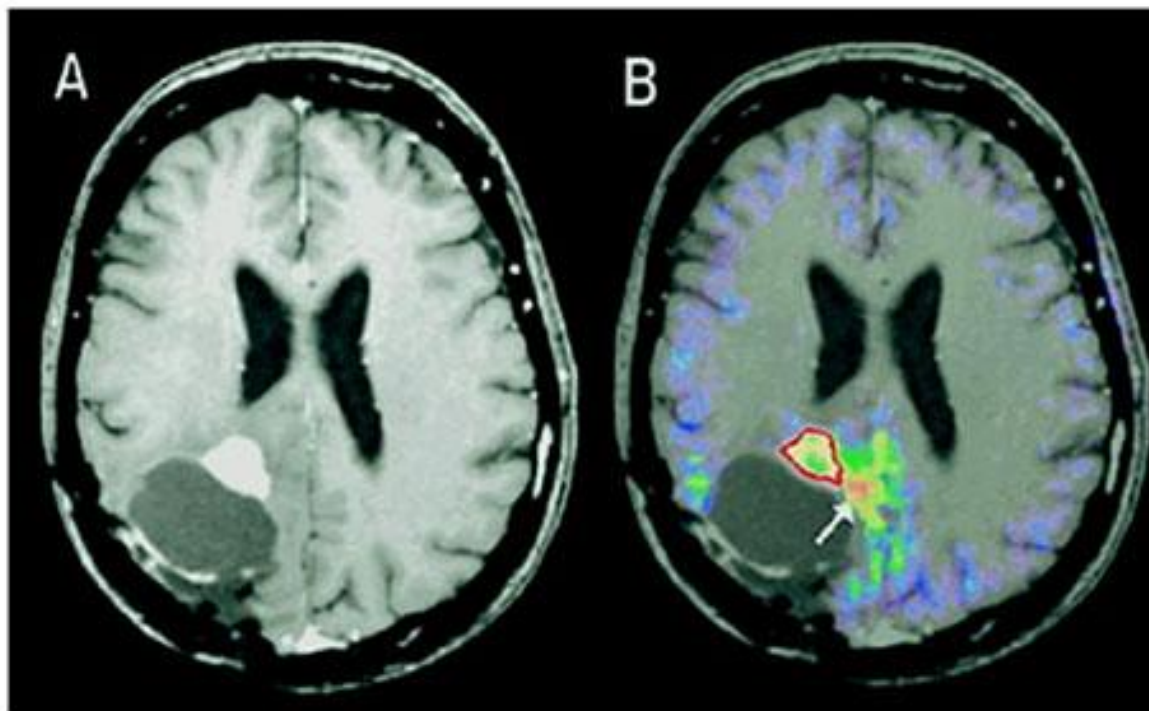


Mapping of brain function



Task-related functional
PET investigations

Methionin PET and MRI fused imaging: size of recurrent tumor after surgery



A, T1-weighted MRI scan with gadolinium-diethylenetriamine penta-acetic acid shows contrast enhancement of the suspected lesion at the mesial wall of the cavity where the tumor was removed. B, fusion of coregistered [11C]methionine PET and MRI shows increased tracer uptake (arrow) outside the contrast-enhancing area (red contour in B corresponds to contrast enhancement in A).



*Thank you
for
your attention!*

Loris Marazzi:
Your brain is your power