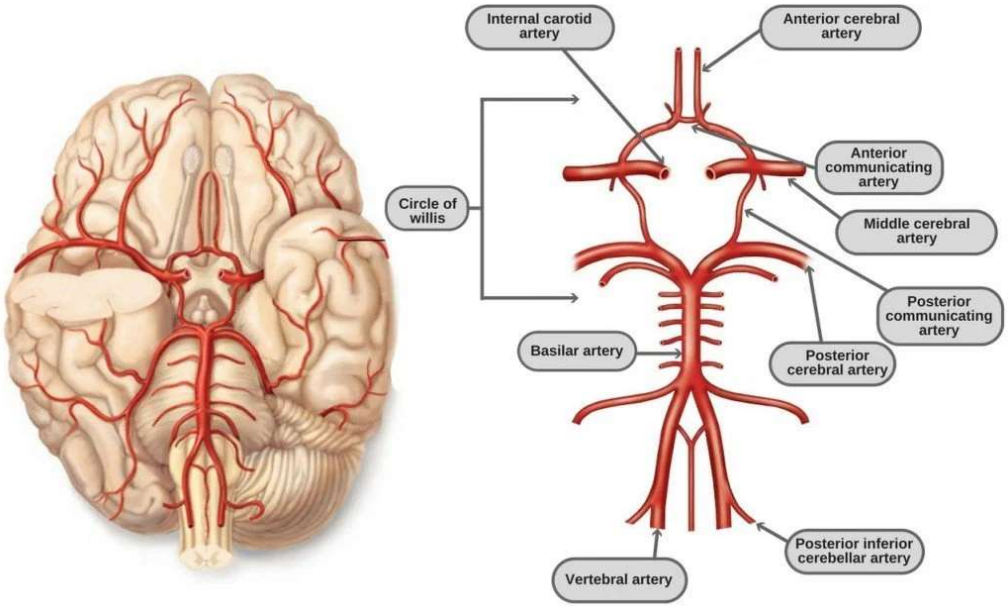
Radionuclide Brain Imaging
Nuclear Neurology

Anatomy and Physiology

- The blood supply to the brain is from four arteries in the neck: the two internal carotid arteries anteriorly, which divide into the anterior and middle cerebral arteries bilaterally; and the two vertebral arteries posteriorly. These join in front of the brainstem to form the basilar artery, which then divides into two posterior cerebral arteries. There are variable communications (anastomoses) between the cerebral arteries called the “circle of Willis” .
- Blood flow to the gray matter is approximately 80 ml/min/100 g of tissue, white matter which receives 20 ml/min/100 g.
- The metabolic substrate of the brain is glucose



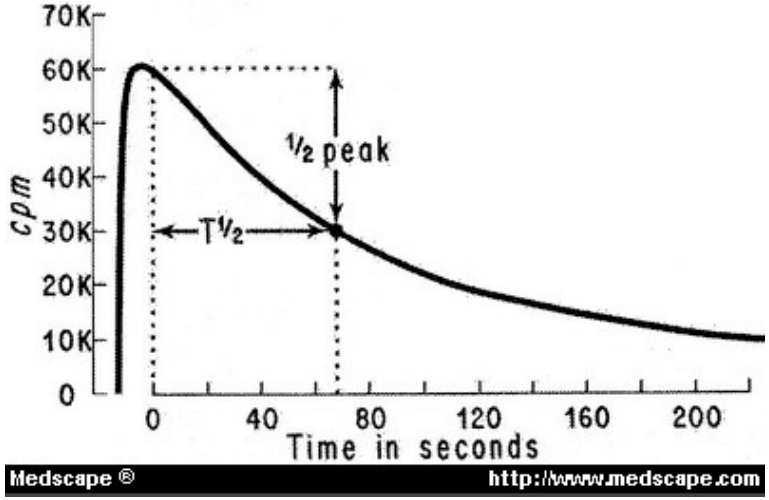
- assessment of blood flow is currently performed not only with the aim of detecting cerebrovascular disorders, but also to assess other diseases of the nervous system that, due to neuronal death or to neuronal loss of function, require less blood supply compared to normal regions.
- reduction of blood flow is secondary to a reduced metabolic demand.
- increase in blood flow is interpreted as a consequence of increased functional activity and this concept is the basis of the neuroactivation studies

Cerebral Blood Flow and Metabolism Tracers

- SPECT radiopharmaceuticals used for measuring regional cerebral blood flow (rCBF) are lipophilic agents which are transported from the arterial vascular compartment to the normal brain tissue compartment by diffusion, and are distributed proportional to regional tissue blood flow. After this first phase of transport the tracers are essentially irreversibly trapped in the tissue compartment. The two major blood flow agents used in brain SPECT imaging are ^{99m}Tc--hexamethylpropylene amine oxime (^{99m}Tc-HMPAO) and ^{99m}Tc-ethyl cysteinate dimer (^{99m}Tc-ECD)), they are lipophylic and are taken up on first-pass cerebral perfusion. Both reach a steady state after a few minutes and remain bound for between two (ECD) and six (HMPAO) hours. This property allows delayed imaging, which can be useful in certain clinical situations.
- Xenon-133 is unique since it is freely diffusable, and not trapped in the tissues.
- The major PET radiopharmaceutical used to measure cerebral perfusion is ^{15}O labeled water
- The use of molecular ^{15}O-oxygen, along with ^{15}O-water permits the assessment of oxygen extraction fraction, cerebral blood flow, and oxygen metabolism
- The assessment of cerebral metabolism can be achieved by PET ^{18}F-FDG

Xe-133 for Quantitative Regional Cerebral Blood Flow

- in brain SPECT imaging has been the development of special software. This allows calculation of tomographically displayed absolute quantification of regional cerebral perfusion (rCBF) in milliliters per 100 g of tissue per minute. This is possible since the clearance of xenon- 133 is linearly proportional to the rCBF, One of the major limitations of xenon-133 SPECT is the relatively low energy of the emission photon, resulting in a significant attenuation and loss of spatial resolution of the central structures of the brain. In addition,.
- Measure cerebrovascular perfusion reserve with rest/stress SPECT brain scans in patients with cerebrovascular disease (CVD) and suffering from TIA
- Xe-133 SPECT detected perfusion asymmetries, even in the mild ischemic group, and therefore is a more sensitive detector of vascular disease.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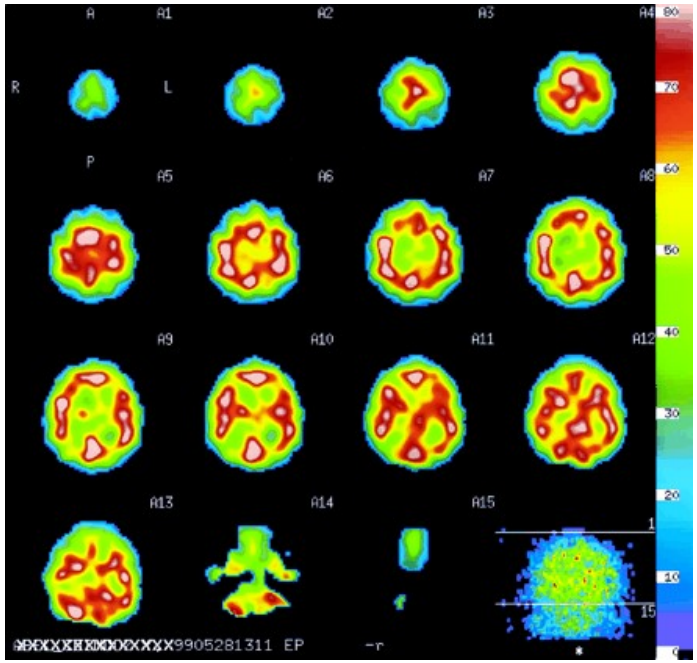
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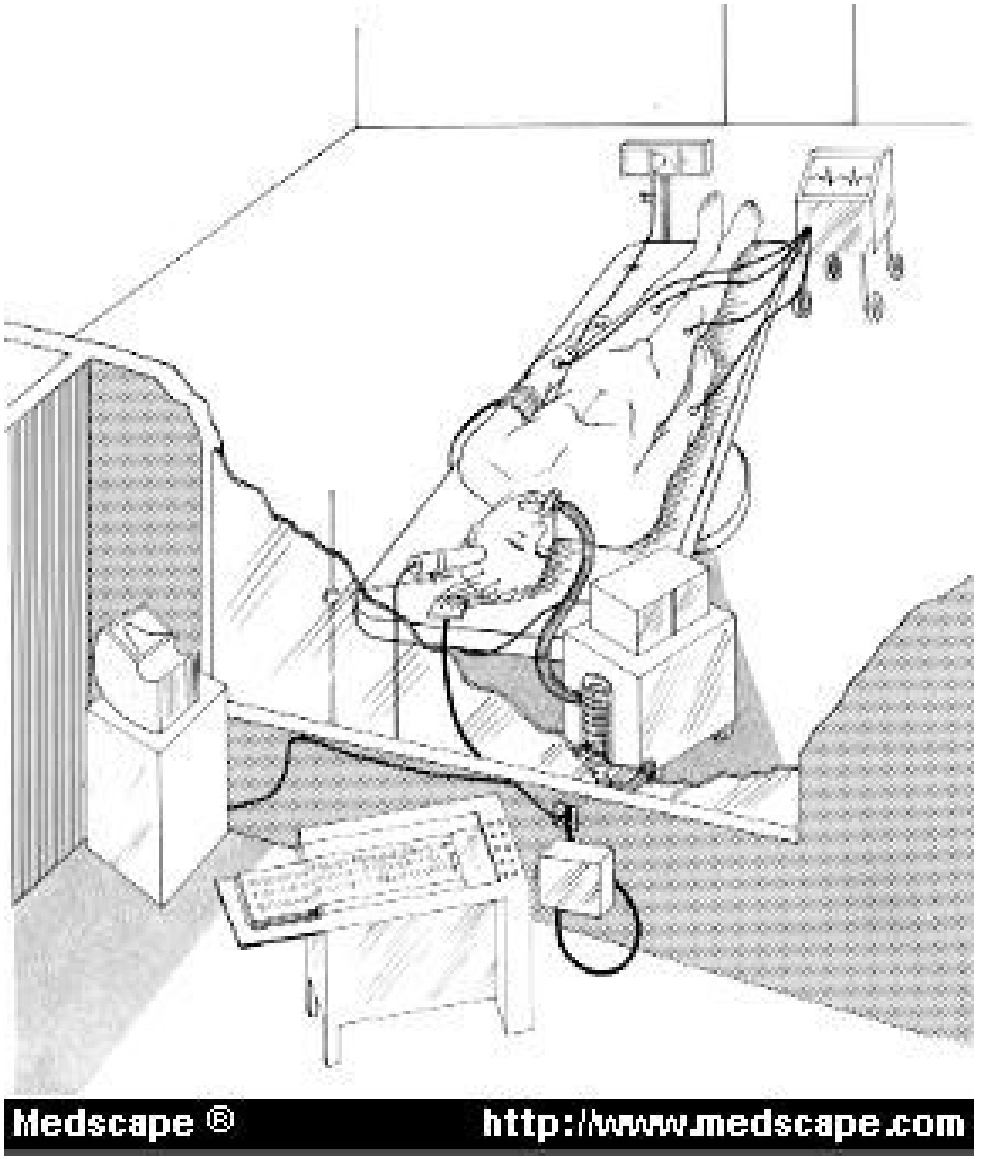
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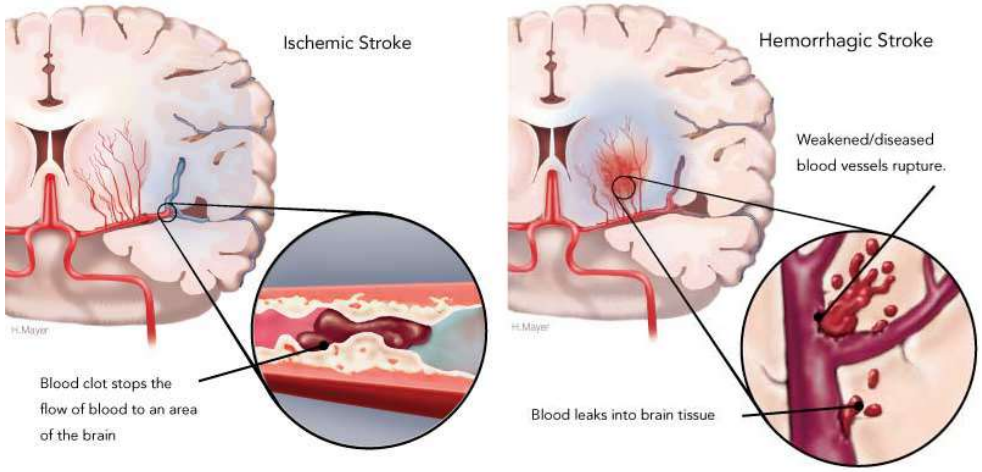
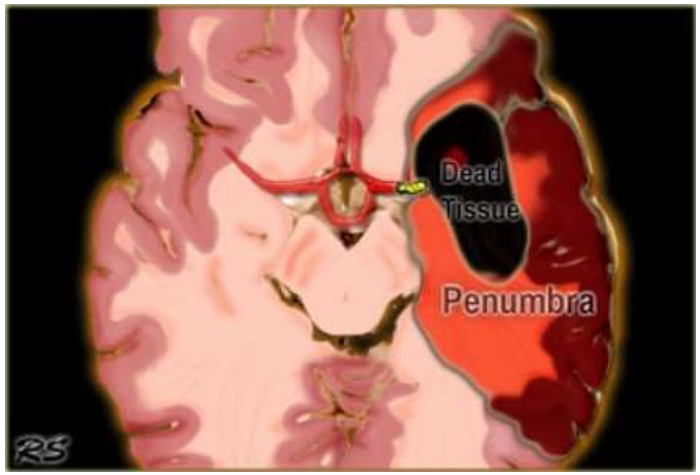
SPECT and PET Brain Imaging in the Evaluation of Cerebrovascular Disease

- CT and MRI have largely replaced SPECT and PET, for the detection, differential diagnosis, and prognosis assessment and follow-up of patients with acute stroke.
- Brain SPECT is still used in the assessment of complex cases and also for the evaluation of cerebrovascular reserve with and without an acetazolamide.
- PET imaging is additionally utilized in the determination of the oxygen extraction fraction (OEF) in patients being considered for corrective carotid artery obstructive disease surgery. Unfortunately, this technique is not widely employed because of the requirement for an on site cyclotron for oxygen-15 production.

- In transient ischemic attacks (TIA), i.e., reversible episodes of temporary focal neuronal dysfunction caused by a transient cerebral hypoperfusion, SPECT perfusion studies within hours of the event demonstrate a persistent perfusion reduction, which in some cases may last for up to several days following the clinical recovery.
- This condition, i.e., persisting hypoperfusion with normal CT and complete clinical recovery termed “incomplete infarction”, may be due to reduced vascular reserve, i.e., the capacity of the cerebral circulation to comply to increases in metabolic demand with vasodilatation. When this occurs, vascular reserve, an important predictor of stroke, can be measured in individual patients by assessing perfusion before and after pharmacologic challenge.
- Acetazolamide, 5% CO_2, or adenosine administration cause vasodilatation and increase blood volume and perfusion only in areas supplied by normal vessels

- The aim of imaging in acute stroke is to demonstrate brain which has reduced perfusion, but which has not yet undergone irreversible infarction (the “ischemic penumbra”) and exclude intracranial hemorrhage. This method has been used to select acute stroke patients for intervention with thrombolysis





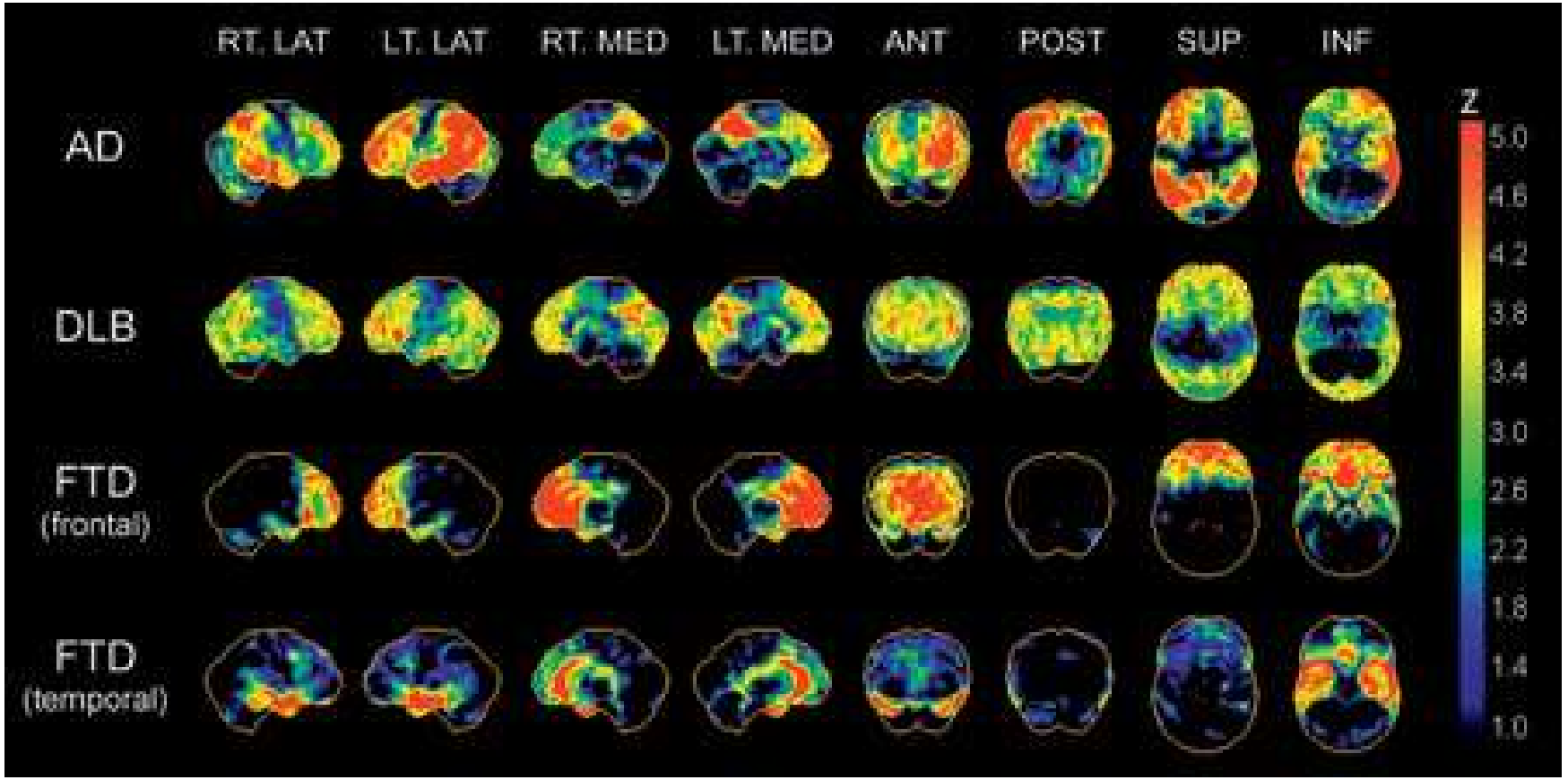
SPECT and PET Brain Imaging in the Evaluation of Dementia

- The rationale for imaging as a diagnostic tool for Alzheimer's disease is based on the disease associated reduction in metabolic brain activity, which can be visualized on both F-18-FDG brain PET and Tc-99m- HMPAO or Tc-99m-ECD brain SPECT. There is a reduction of brain glucose metabolism identified on PET due to reduced neuronal metabolism.
- PET is finding an increasing role in the early detection, differential diagnosis, prognosis and follow-up of dementia. Both ^{18}FDG and H2^{15}O PET have been studied in AD and demonstrate metabolic and perfusion defects respectively in the typical posterior temporoparietal areas.
- Glucose metabolism imaging with 18F-FDG is the most sensitive and specific imaging modality available today for the diagnosis of Alzheimer's disease (AD). sensitivity as high as 95%–97% and a specificity of 100%, in discriminating patients with probable AD from normal subjects, probable AD patients have reduced glucose utilization in the posterior temporo -parietal lobe cortex

- high sensitivity of 18F-FDG PET in the early detection of AD. Many subjects with AD have already an abnormal PET on the initial examination performed for mild memory loss, hypometabolism actually precedes both symptoms and the clinical diagnosis of AD.
- Pick's disease, and in patients with a neuropsychometric suggestion of frontal dementia, 18F-FDG PET reveals the greatest reduction in the frontal and anterior temporal association cortical regions
- 123I-IBVM SPECT method for studying AD revealed losses of cholinergic cortical innervation.
- Pittsburgh Compound B, a PET tracer, has been developed to bind to amyloid deposits in the brain

- Dementia with Lewy bodies (DLB) is thought to be the second most common primary dementia after AD. Global and visual cortical involvement has also been found in DLB using FDG PET
- Frontotemporal Dementia demonstrates anterior perfusion defects involving the frontal and anterior temporal lobes, with preserved perfusion posteriorly,
- Vascular dementia is the second most common form of dementia and may coexist with Alzheimer's disease or other dementias, so-called "mixed dementias". Traditionally it has been associated with a stepwise deterioration clinically and the presence of one or more supratentorial infarcts on structural imaging. HMPAO SPECT may demonstrate multiple patchy perfusion defects

Pet Scans Detect Dementia and Differentiate Between Alzheimer, Frontotemporal, and Lewy Bodies Dementia



SPECT and PET Brain Imaging in the Evaluation of Brain Tumors

- Brain tumors accounting for about 2% of all adult malignancies.
- Overall, gliomas make up over 90% of all adult brain.
- In children are typically infratentorial with medulloblastomas,the most common.
- In addition, there are also many secondary ormetastatic tumors that may involve the brain via the systemic circulation.
- Since the first introduction of FDG-PET imaging, it has been recognized that the technique is very sensitive for detecting high-grade gliomas with an overall accuracy in the range of 90–95%.
- In addition, the degree of uptake in tumors cells has been shown to correlate directly with the degree of malignancy noted on histopathology.

Brain SPECT Imaging

- The SPECT radiopharmaceutical can be divided into a number of broad groups including:
- regional cerebral blood flow compounds [99mTc]HMPAO and [99Tc]ECD;
- cationic compounds thallium-201, [99mTc]MIBI, [99mTc]- tetrofosmin;
- labeled amino acids [123I]iodo-methyltyrosine
- labeled antibodies;
- labeled somatostatin analogs
- apoptosis compounds [123I]annexin

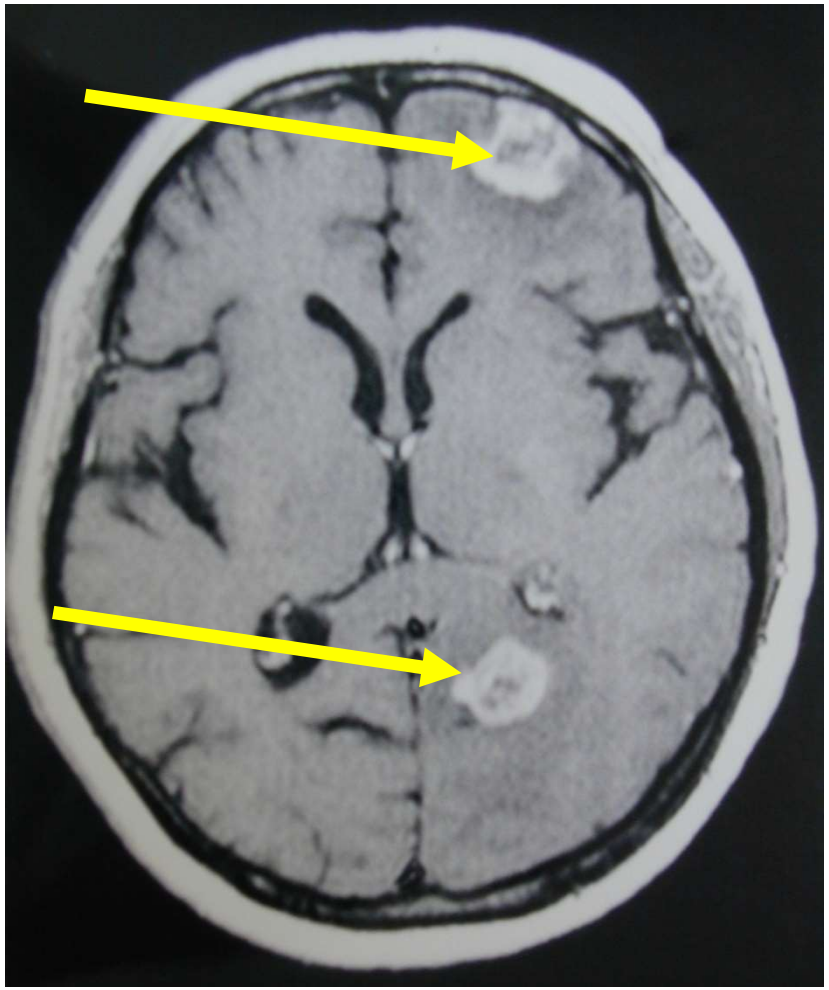
Brain PET Imaging

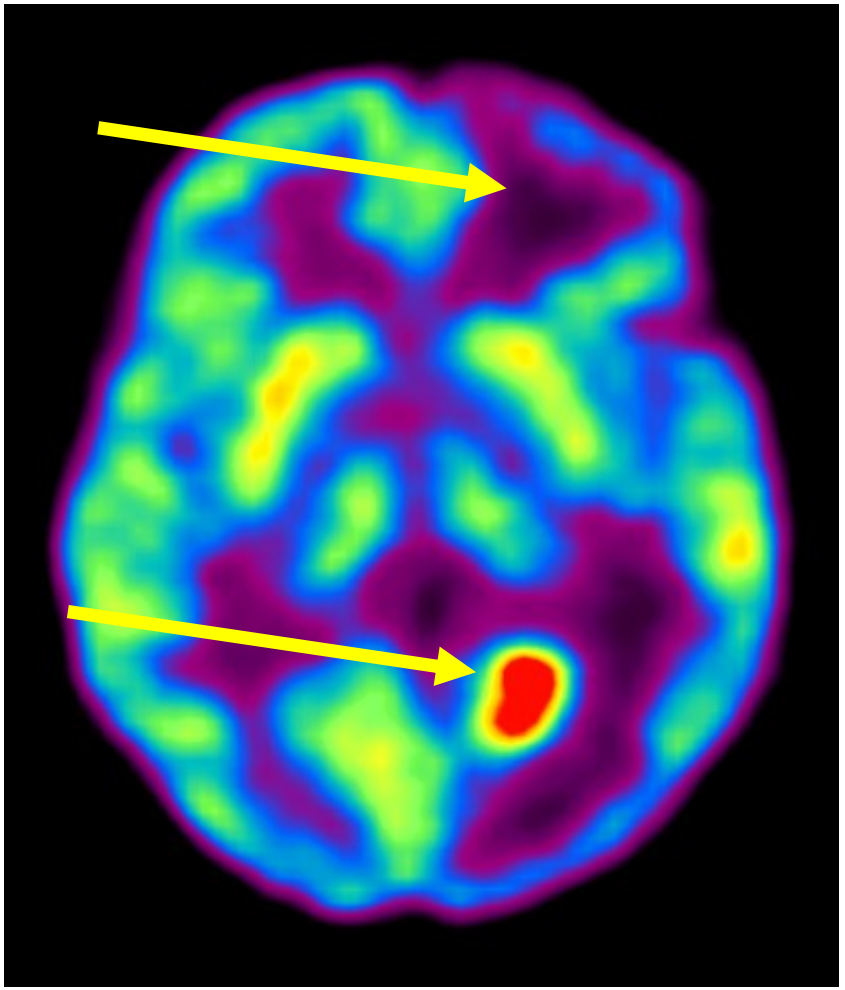
- is most commonly performed with FDG.
- FDG-PET is of value for tumor detection; defining tumor extent and degree of malignancy; as well as in the assessment of tumor response, and differentiation of viable tumor versus radiation necrosis
- [11C]methionine (MET), which is incorporated into the tumor protein synthesis pathway, is very useful for detection of low-grade brain tumors (more accurate than FDG)
- Other compounds, including [11C] and [18F]choline and [18F]fluoro-thymidine, are currently in clinical trials to further define their clinical efficacy.

- Since the very early days of PET brain imaging, it has been recognized that the methodology is less accurate for the detection of histologic low-grade tumors. In part, this lower accuracy rate is due to the high cortical gray matter of FDG often surrounding the actual tumor. The absolute uptake of labeled glucose is also confounded by uptake in areas of inflammation and/or infection including the tumor itself during and immediately after treatment. Delaying the initial scan 6–8 weeks after completion of treatment and the performance of serial imaging at a number of time points post FDG administration are of some value for improving the accuracy of tumor detection
- Labeled amino acids, in particular [11C]methionine (MET), can often be complementary to FDG imaging. MET has an improved accuracy rate for detecting lowgrade tumors and is not hampered to the same degree as FDG by uptake in adjacent gray matter of the surrounding brain

- Thallium-201 in the form of thallous chloride is a cyclotron produced radiopharmaceutical shown to have affinity for brain tumors as early as the 1970s
- Although more commonly used as a myocardial perfusion imaging agent, thallium has high sensitivity for detection of new, recurrent or residual viable tumors, which are difficult to differentiate from post-radiation necrosis and edema on CT or MRI.
- Thallium is normally taken up by regions of the brain which do not have a blood brain barrier (BBB) such as the pituitary gland, pineal gland, and are minimally taken up by the choroid plexus
- Brain SPECT imaging employs the tracer thallium-201 to detect new, residual, or recurrent viable tumor due to the fact that there is transport of thallium-201 across the breakdown in the blood brain barrier, and uptake of thallium-201 into regions of hypermetabolism.
- Thallium accumulates in the residual or recurrent viable tumor cells in proportion to malignant grade and total viable tumor bulk.

FDG PET – brain tumor post th
two foci on CT, only one viable tumor





- Tc-99m-Hexakis-2-methoxy-2-isobutyl isonitrile (Tc-99m-sestamibi or MIBI) is used extensively in myocardial perfusion imaging. Normal brain tissue shows minimal uptake of 99mTc-MIBI. The normal physiologic distribution in the pituitary gland, choroid plexus
- In brain tumors the mechanism of tumor uptake is also thought to be dependent on mitochondrial activity and the presence of P-glycoprotein.

PET tracers commonly used in neurooncology

	probe for
^{18}F-fluorodeoxyglucose (FDG)	glucose metabolism
^{11}C-methionine (MET)	protein synthesis
^{18}F-fluoroethyltyrosine (FET)	protein synthesis
^{18}F-choline	phospholipide synthesis
^{18}F-fluorothymidine (FLT)	DNA synthesis
^{18}F-DOPA	protein synthesis
^{68}Ga-DOTA-TOC	somatostatine receptors

Other PET tracers for brain tumors

	probe for
^{11}C-acetate	oxidative metabolism
^{64}Cu-DOTA-VEGF *	angiogenesis
^{15}O-H_2O	blood flow
^{18}F-fluoromisonidazole (FMISO)	hypoxia
^{64}Cu-cetuximab	EGF receptor *

* VEGF - vascular endothelial growth factor EGF - endothelial growth factor

> 90% of neurooncologic PET examinations are based on ^{18}FDG

FDG advantages

- Good corelation of uptake with histologic grade of the tumour
- Status HE barrier does not affect uptake

FDG limitations

- Intense uptake occurs in normal brain
- Inflammatory lesions take-up FDG

Aminoacid tracers: ^{11}C-MET, ^{11}C-FET

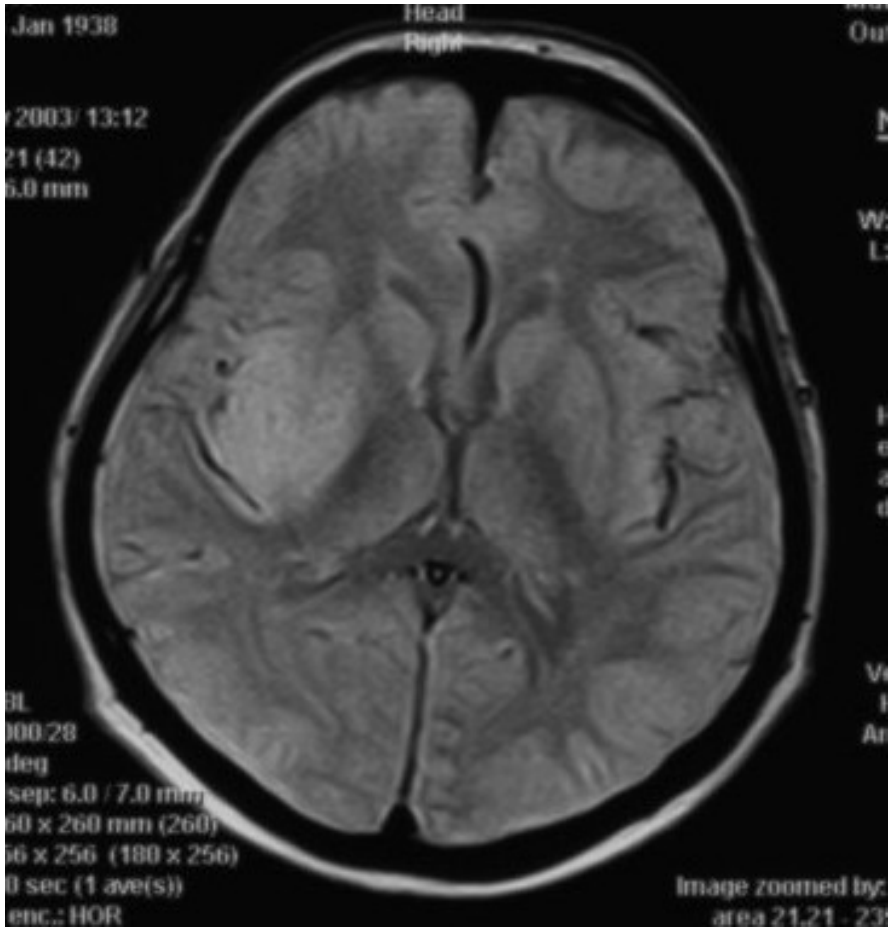
Advantages

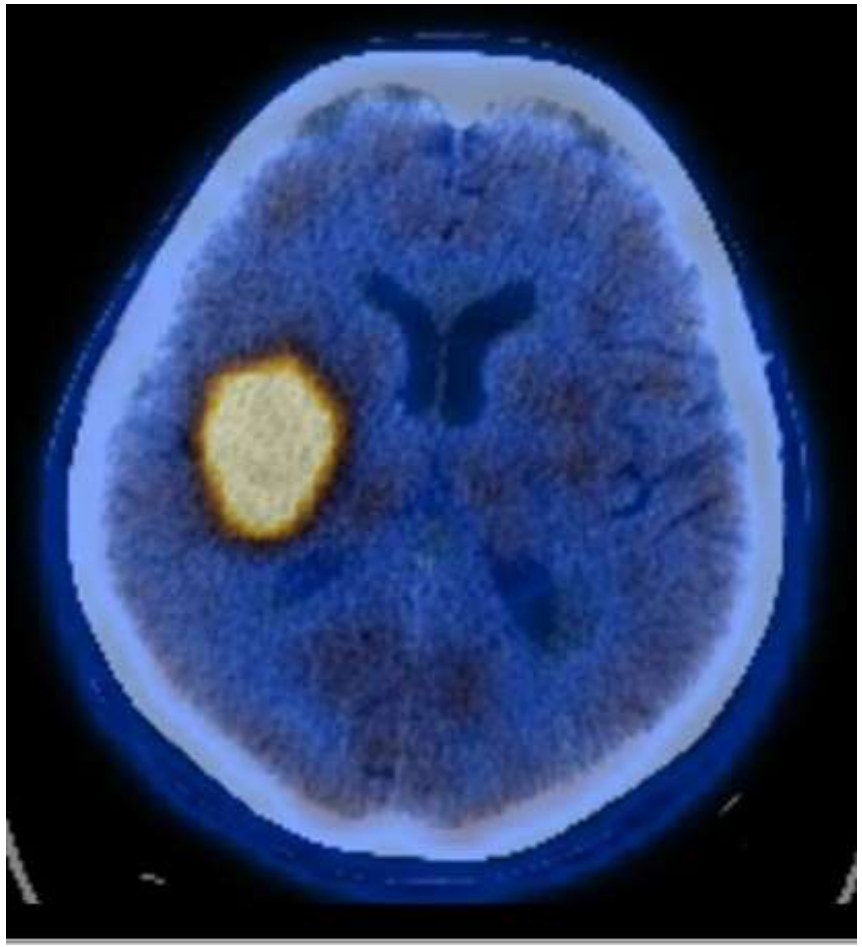
- very low uptake in healthy brain tissue
  - higher sensitivity than FDG, especially for low-grade gliomas
  - better delineation of tumour boundaries
- less than FDG taken-up by inflammatory lesions

Limitations

- tumour uptake weakly correlated to malignancy grade
- disruption of HE barrier (caused by radio-Th) increases the uptake of aminoacids in brain tissue
- limited availability (cyclotron)

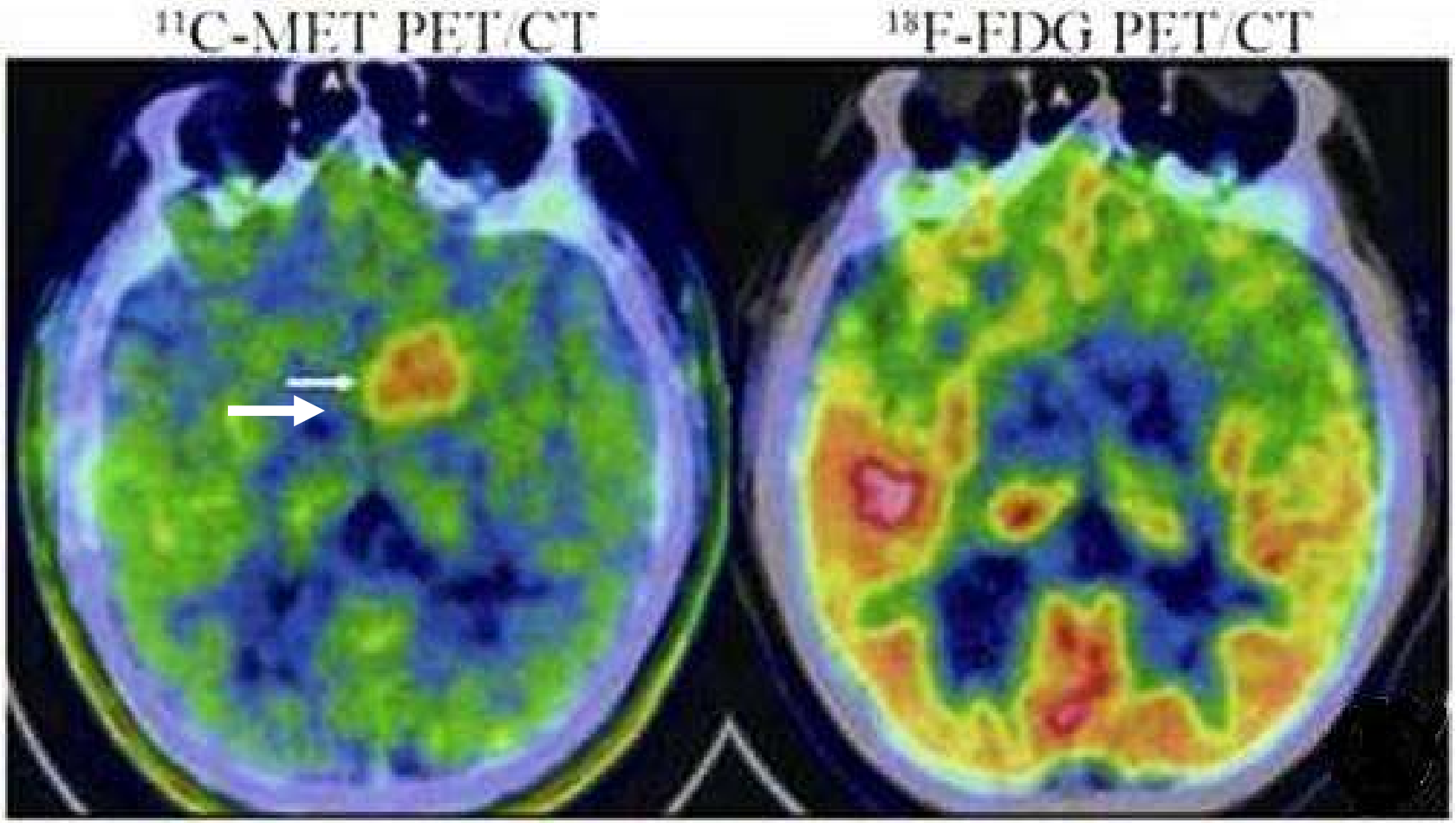
Malignant astrocytoma ^{11}C-MET





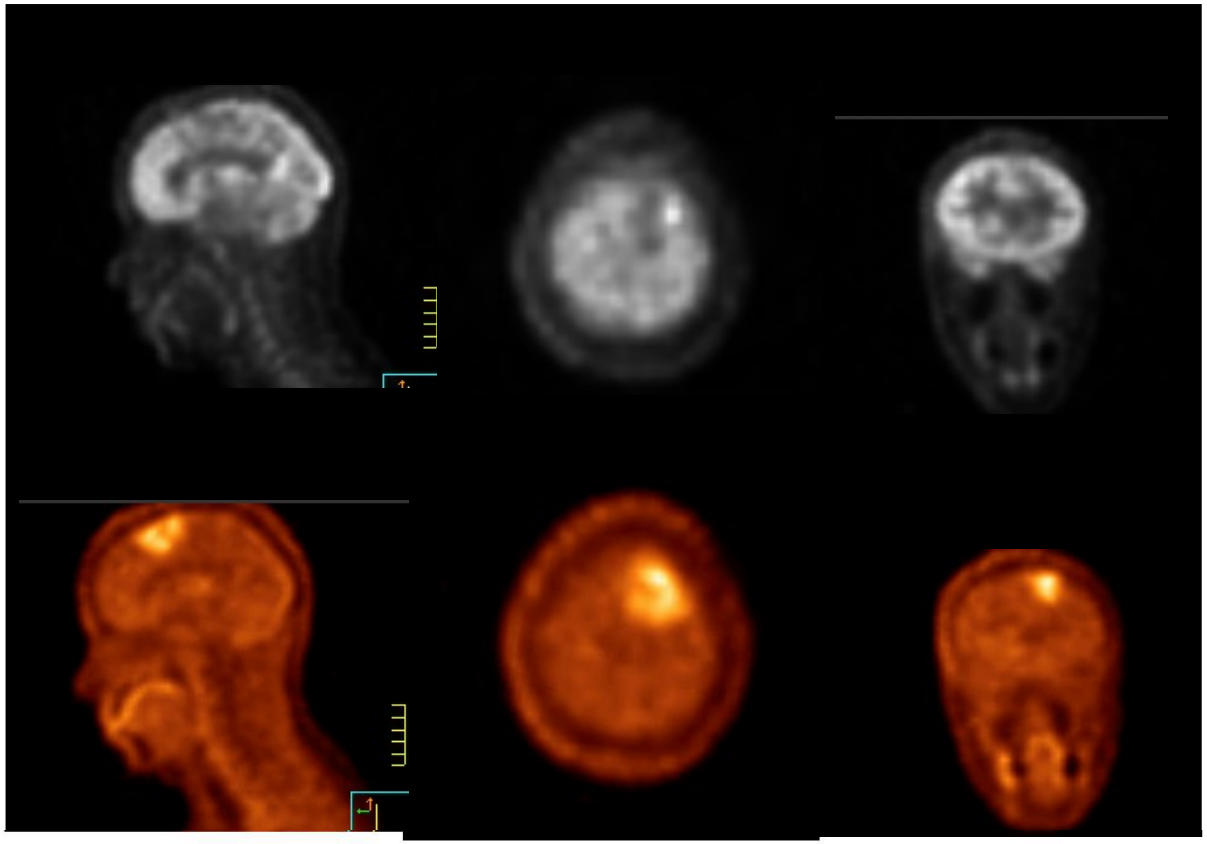
MR **PET/CT**

Low grade glioma



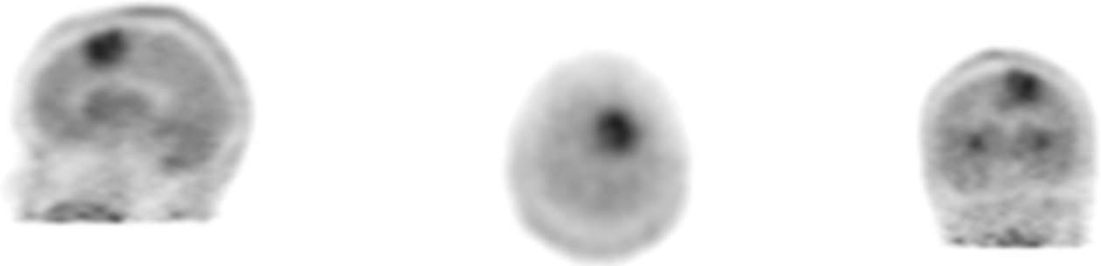
Which radiopharmaceutical for post-treatment surveillance of gliomas ?

Left frontal oigodendri-oglioma, grade II. Operated 6 years before the onset of epilepsy.



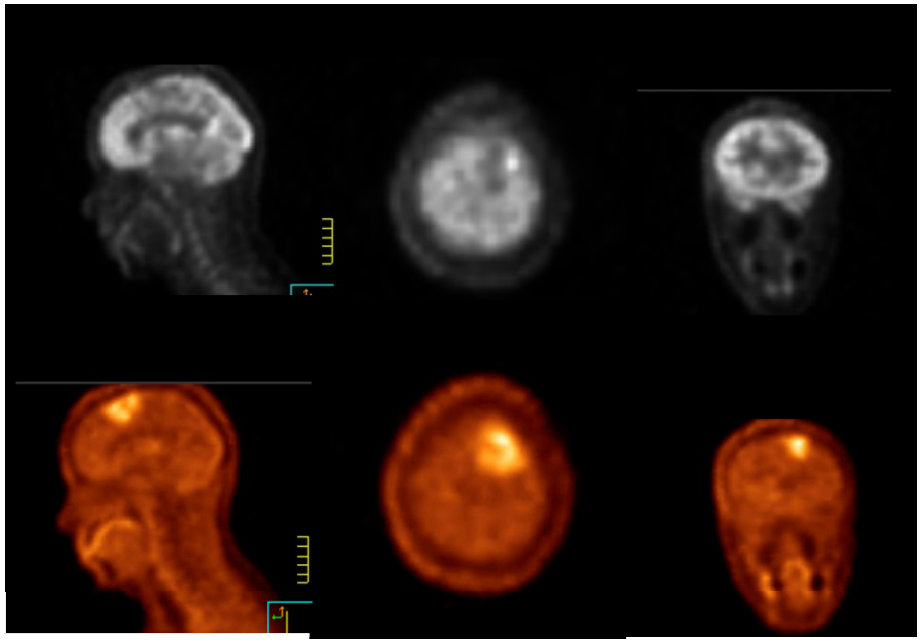
FDG

FET



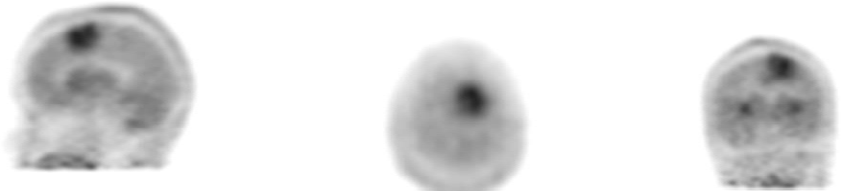
FDOPA

Which radiopharmaceutical for post-treatment surveillance of gliomas ?



FDG

FET



FDOPA

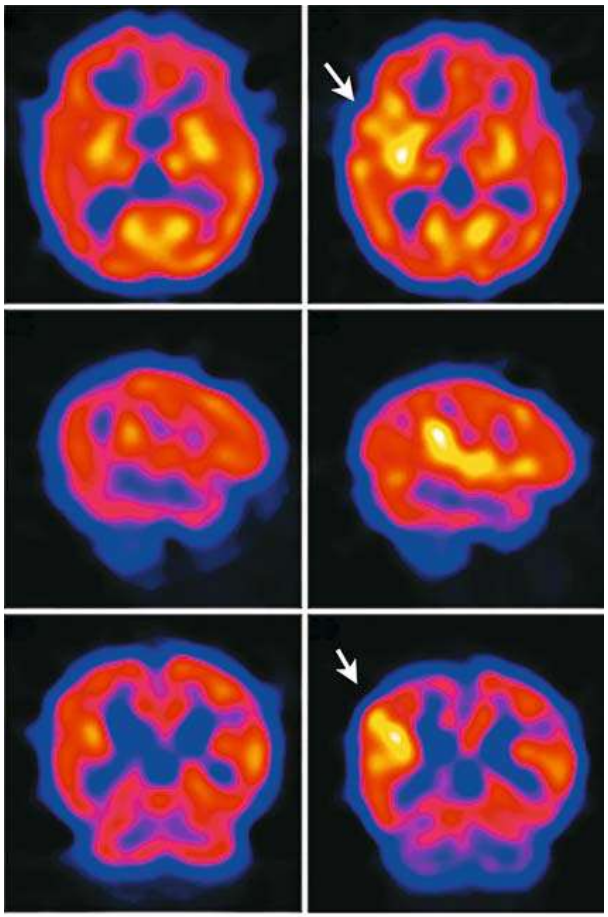
Left frontal oigodendri-oglioma, grade II. Operated 6 years before the onset of epilepsy.

SPECT and PET Brain Imaging in the Evaluation of Seizure Disorders

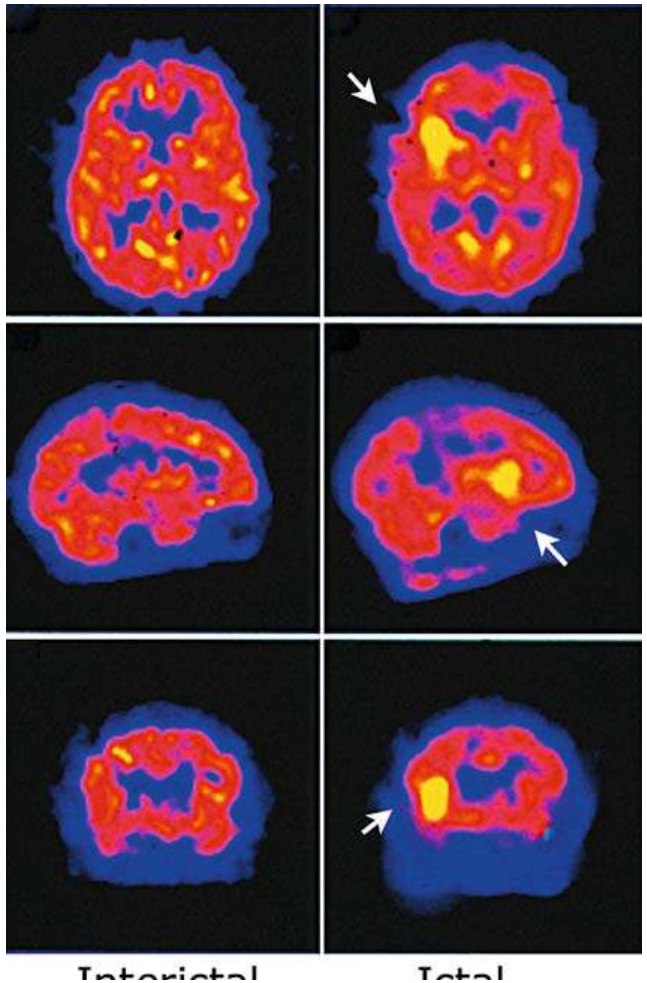
- The optimum brain SPECT method for localizing a seizure focus is to perform ictal and interictal imaging studies, on separate days, followed by subtraction of the co-registered images. This method or some variation is reported to have an accuracy rate in the range of 89–94%
- the patient should be observed on a continuous video EEG monitoring system in a seizure disorder unit. The intravenous injection of the SPECT radiotracer should occur in less than 2 min from the time of the seizure so as to ensure that a diagnostic SPECT study, representative of the ictal state, is obtained.
- for an interictal SPECT study it is important that the patient be documented as being seizure-free for at least 24 h prior to injection of the radiotracer.
- The ictal SPECT study reveals a localized area of increased radiotracer activity at the site of the seizure activity that is reflective of the increased rCBF and metabolism present at the time of ictus.
- interictal study reveals decrease in rCBF at the seizure site.

- PET Brain Imaging FDG-PET brain studies are also utilized to evaluate seizure disorder patients in the interictal state. Similar to interictal SPECT, this technique identifies the interictal seizure focus as an area of focal hypometabolism.
- The most commonly employed neuroreceptor imaging technique employed in the evaluation of epilepsy is the GABA receptor [11C]flumazenil. This compound has been reported by a number of investigators to be a very reliable method for identifying seizure foci

Eight-month-old with intractable seizures. Ictal 99mTc-ECD SPECT reveals increased brain flow in the epileptogenic zone (arrows).



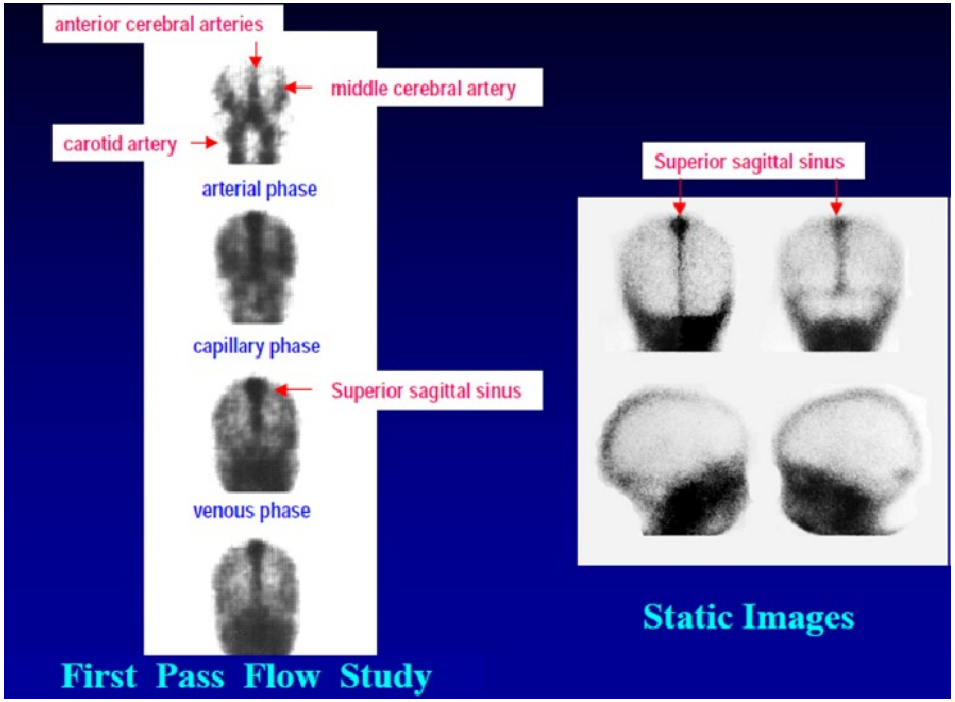
Interictal and ictal 99mTc-ECD SPECT reveals focal ictal hyperperfusion in the right parietal region (arrows).



Cerebral Angiography

If a non–brain-binding agent such as ^{99m}Tc-DTPA is used, static planar images are acquired in anterior (and posterior, if helpful) and 1 lateral view for 500,000 to 1,000,000 counts per view

In a patient with normal intracranial flow, the paired midline anterior cerebral arteries and laterally situated middle cerebral arteries appear as a three-pronged “trident-”like structure



Cerebral Angiography

- ^{99m}Tc pertechnetate scan: The pertechnetate (^{99m}TcO4-) ion in technetium (Tc) pertechnetate binds to plasma proteins, quickly moves into the extra-cellular space and distributes itself like the chloride (Cl-) ion in various organs except the normal brain because of the blood brain barrier (BBB). Thus, negligible uptake of the isotope by the normal brain prevents its effective visualisation by isotope scan, unlike other organs-

- Lesions: Any pathological process can break down the BBB, allowing the ^{99m}TcO4- ion to localise in the area as a 'hot' spot (positive scan), contrasting with the low uptake in the normal areas of the brain with intact BBB (negative scan). The differences in uptake are accentuated on immediate and/or delayed scans.

- Vascularity: Tumours, inflammatory masses, abscesses, infarction, intra- and extra-cerebral haemorrhage all give positive scans. The ^{99m}TcO4- ion localisation is not specific for any lesion but occurs in any lesion where disruption of the BBB and the vascularity of the lesion allows high lesion-to-brain distribution ratio.

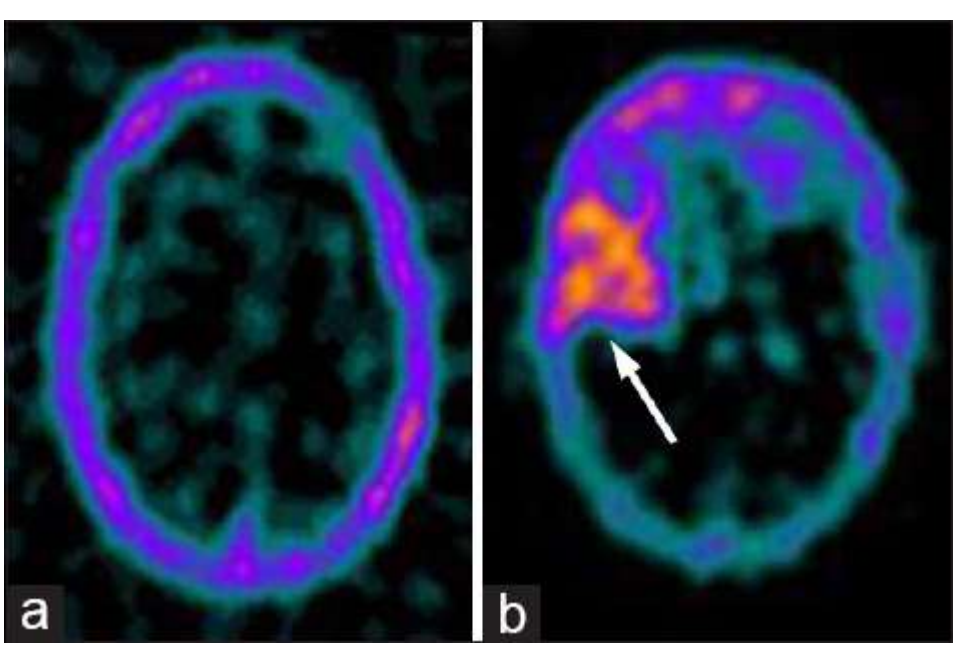
- ^{99m}Tc DTPA scan: Administered IV, it is used commonly in renal scans, but it is also used in brain and lung scanning. Being lipophobic, it does not cross the blood brain barrier. Therefore it is more useful as a non-specific angiographic radionuclide in brain scans.

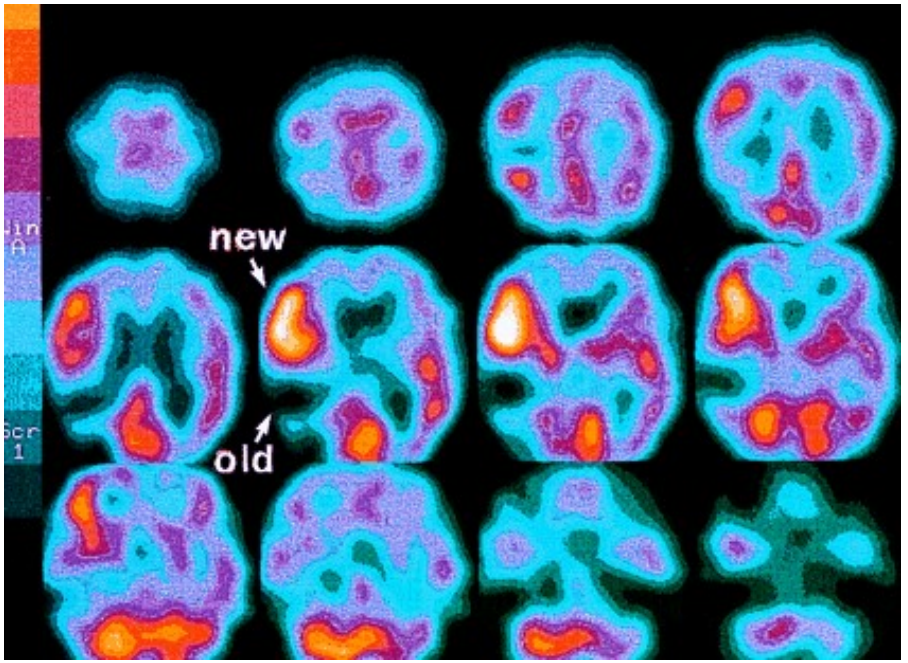
- Space-occupying lesions (SOL) such as meningioma, acoustic tumor, malignant glioma and brain abscess appear particularly prominent in scan. Since this technique images the entire head as opposed to slices, accurate localization of lesions with respect to external observable landmarks is possible. On the other hand, in contrast to CT or MRI scan, radio-nuclide scan provides very little anatomical detail.

- Vascular lesions are divided into; infarcts; hematomas; and arterio-venous malformations (AVM).
- Some infarcts may be successfully imaged in their sub-acute stage and they are often positive especially in the 2nd or 3rd week. Many hematomas are positive in the sub-acute stage (first week), remain positive for several weeks and then return to normal on radio-nuclide scan.

- Dynamic radio-nuclide angioscan:This involves obtaining rapid (1-second interval) images shortly after an IV bolus injection of 9^{9m}Tc. It depicts blood flow through the brain and is particularly useful in patients with AVM. In this condition, gamma camera viewing of the posterior of the head and neck shows;
- (a) early appearance of radioactivity over the lesion (typical of AVM) compared to rest of the brain;
- (b) higher peak density of gamma emission and;
- (c) delayed washout of radioactivity in the delayed images.
- This can be compared with static scan images to confirm the increased amount of tracer localised in the region of AVM.

Cerebral Angiography-scan





a) Normal scan b) cerebral infarct

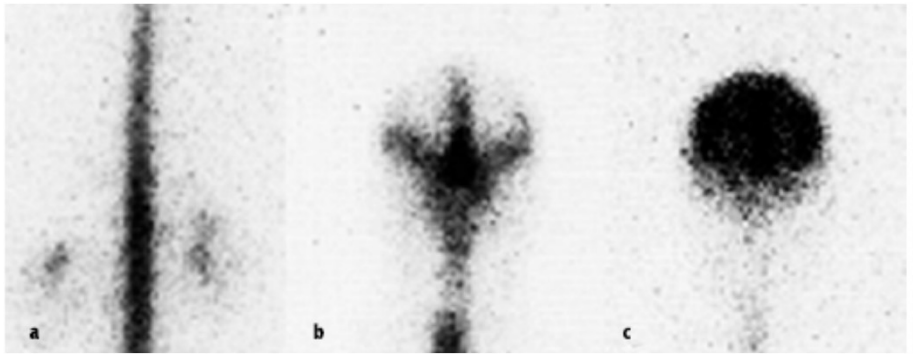
Radionuclide Cerebrospinal Fluid Flow Studies

- **Radionuclide cisternography** is primarily used to track CSF flow from the region of the lower level lumbar spine up to the convexity of the brain where CSF is reabsorbed. Under normal conditions, CSF is secreted by the choroid plexus located in the lateral ventricles, into the intraventricular system. The CSF then flows out of the ventricular system into the intrathecal space surrounding the brain and spinal cord.
- The normal pattern of CSF flow, after leaving the ventricles, is both into the spinal canal and around the brain. CSF flows retrograde from the spinal canal to the basilar cisterns, through the sylvian fissures and over the convexity of the brain where it is absorbed in the arachnoid villi located in the parasagittal regions
- **Radionuclide ventriculography** is procedure used to check the patency of the afferent and efferent limbs of a ventricular shunt as well as function of the shunt pump. ^{99m}TcDTPA is the radiotracer typically used for this procedure

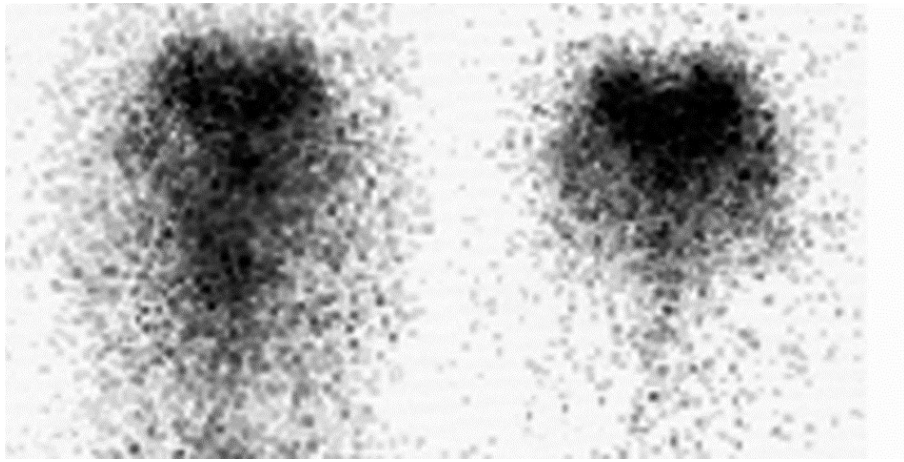
- Radionuclide cisternography involves the injection of radiotracer into the intrathecal space usually at the level of the lumbar spine.
- 111In-DTPA is the most commonly used radiopharmaceutical. The typical dose, which is prepared in a small volume <1 ml ≈ 18.5 MBq. The dose is administered using a small gauge spinal needle so as to avoid leakage back over the injection needle tract. Following administration of the radiotracer, the retrograde passage of CSF is tracked using the gamma camera.
- Typically, the radiotracer arrives at the level of the basilar cisterns by 4 h and then progresses around the brain by two pathways up to convexities where CSF re-absorption occurs by 24 h. The usual imaging times are at 4–6, 24 and, if necessary, 48 h.

- The type of information that is available from radionuclide cisternography in the communicating hydrocephalic patient is useful to the neurosurgeon in helping to decide on the type of shunting procedure to be performed. In particular, radionuclide cisternography is very informative in normal pressure hydrocephalus, a form of communicating hydrocephalus, where the opening CSF spinal tap pressure level is within the normal range. Radionuclide cisternography when combined with surgical packing is also, on occasion, very helpful in identifying the presence and site of a CSF leak

Radionuclide cisternography



Normal CSF flow pattern: Images at 2 h (a) reveal radiotracer, in CSF, ascending up the thoraco-lumbar spinal canal; at 6 h (b) the radiotracer is in the basilar cisterns and at 24 h (c) the radiotracer is being reabsorbed in the arachnoid villi at the convexity of the brain



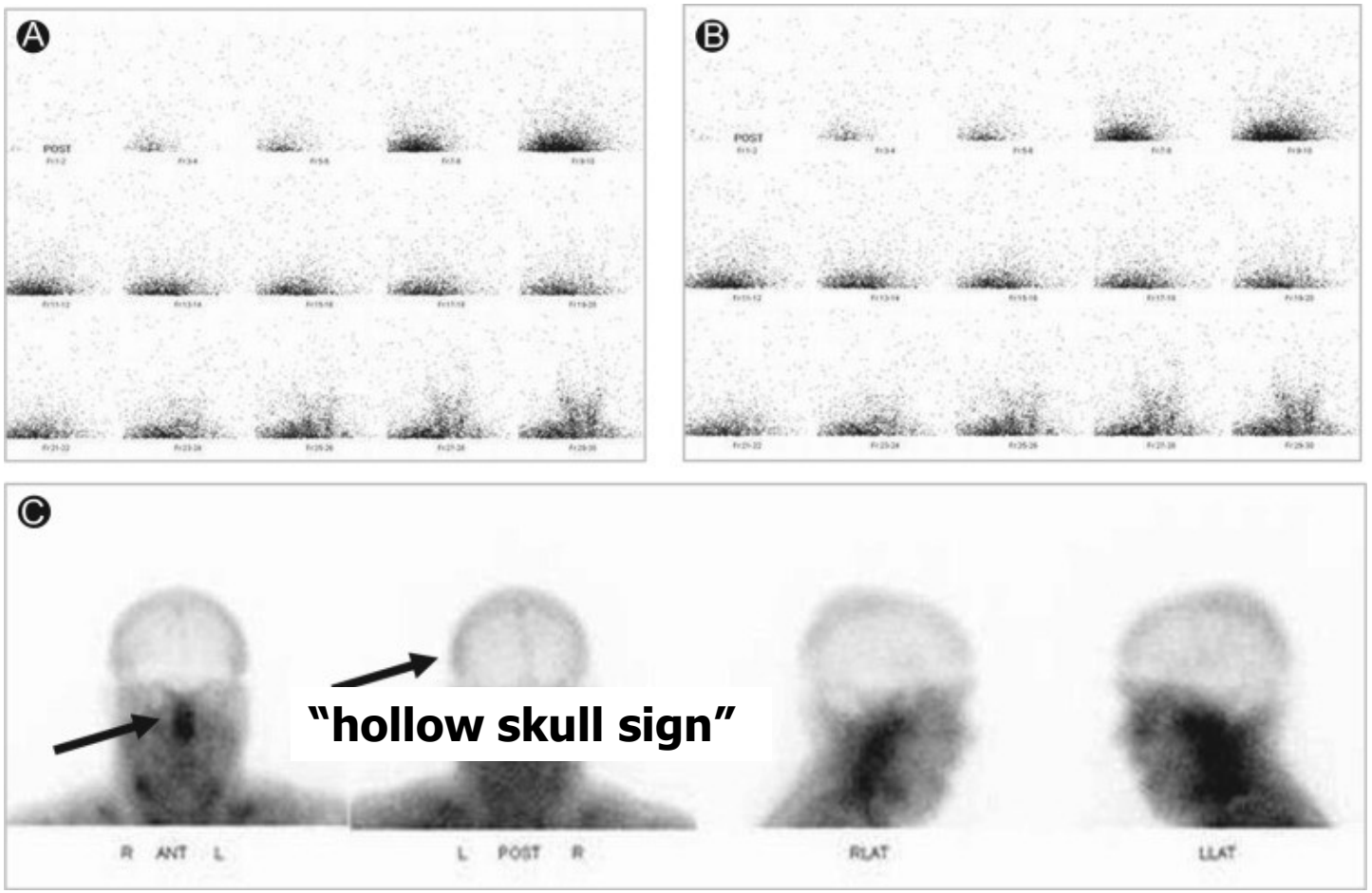
Normal pressure hydrocephalus pattern:and at 48 h persistence of radiotracer in the lateral ventricles, “ventricular stasis” and no movement of the radiotracer beyond the basilar cisterns consistent with
extra-ventricular obstruction to CSF flow

Brain Death Scintigraphy

- Brain death is defined as the irreversible loss of all brain and brainstem functions including the capacity to breathe, even though the heart continues to beat and spinal functions may persist.
- The concept that brain death is equivalent to death of the individual has been widely accepted. The diagnosis of brain death is primarily clinical (apnea, deep coma, loss of all
- brain stem reflexes). Confirmatory tests including cerebral angiography, brain scintigraphy, electroencephalography (EEG) and transcranial Doppler can be used to confirm the irreversibility of brain death in the presence of confounding factors such as hypothermia or drug intoxication, especially when the clinical history is unknown.
- Brain scintigraphy is not affected by centrally acting drugs such as the barbiturates. In particular, brain scintigraphy with lipophilic tracers such as [99mTc]HMPAO hexamethylpropylene amine oxime) and [99mTc]ECD (ethyl cysteinate dimer) that cross the intact blood brain barrier and are retained in the brain has the advantage of demonstrating absence or presence of brain parenchymal perfusion.

- The procedure guideline for brain death scintigraphy published by the Society of Nuclear Medicine states that there is no clear evidence that brain-specific tracers such as [99mTc]HMPAO and [99mTc]ECD are more accurate than traditional nonspecific agents such as [99mTc]DTPA (diethylene-triaminepenta-acetic acid).
- Complete absence of brain perfusion on brain scintigraphy with [99mTc]HMPAO or [99mTc]ECD (“hollow skull sign” Abdel-Dayem et al. 1989) is diagnostic of brain death.

Brain Death Scintigraphy

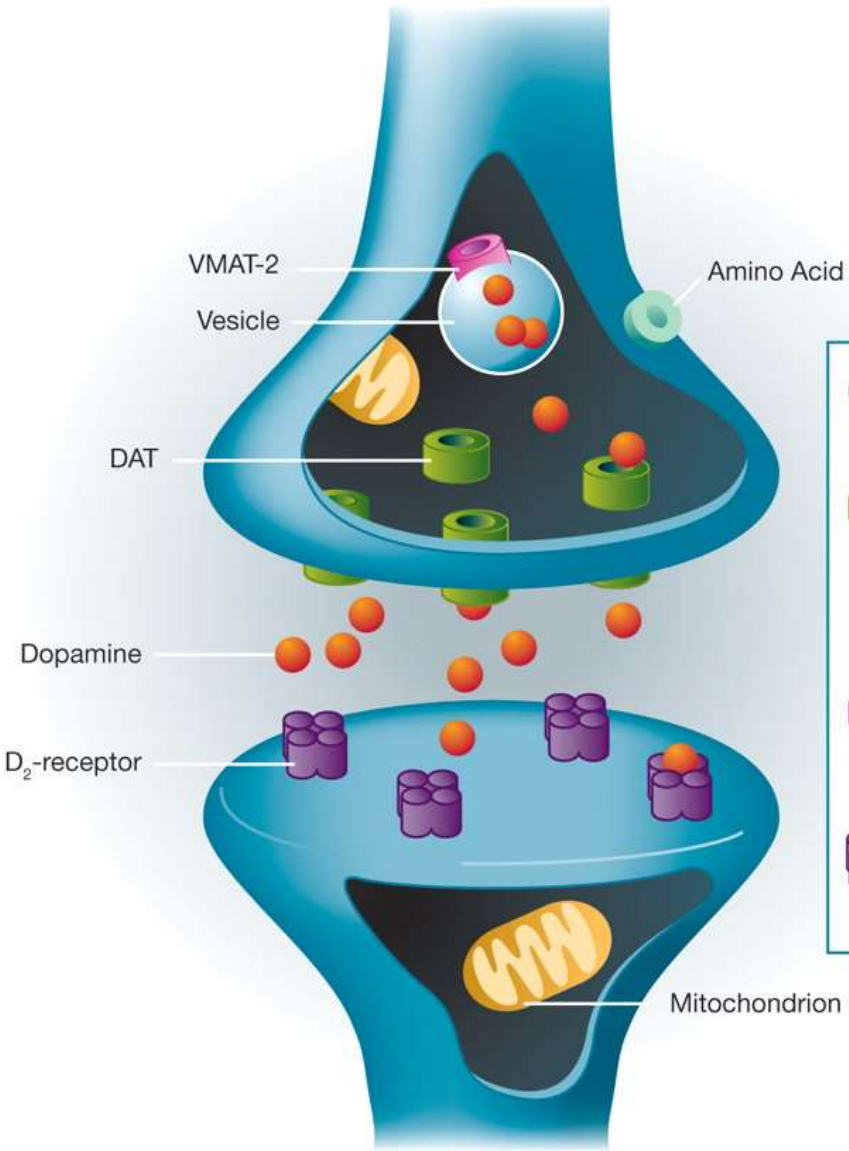


SPECT and PET Imaging of the Dopamine System in Movement Disorders

- The dopamine system is one of the important neurotransmission systems of the central nervous system. There are three major dopaminergic projections in the brain. These three pathways are involved in the control of movement, emotional behavior and endocrine function, respectively.
- PET and SPECT allow quantitative imaging of the dopamine system. They have been used extensively in clinical research to evaluate patients with Parkinson's disease (PD) and other movement disorders. These conditions are characterized pathologically by progressive degeneration of the dopamine neurons that originate in the substantia nigra and project to the striatum.
- There are four different kinds of PET or SPECT radioligands that reflect or bind to: 1 dopamine synthesis, 2 dopamine reuptake sites (dopamine transporter), 3 dopamine receptors and 4 monoamine reuptake or transporter sites.

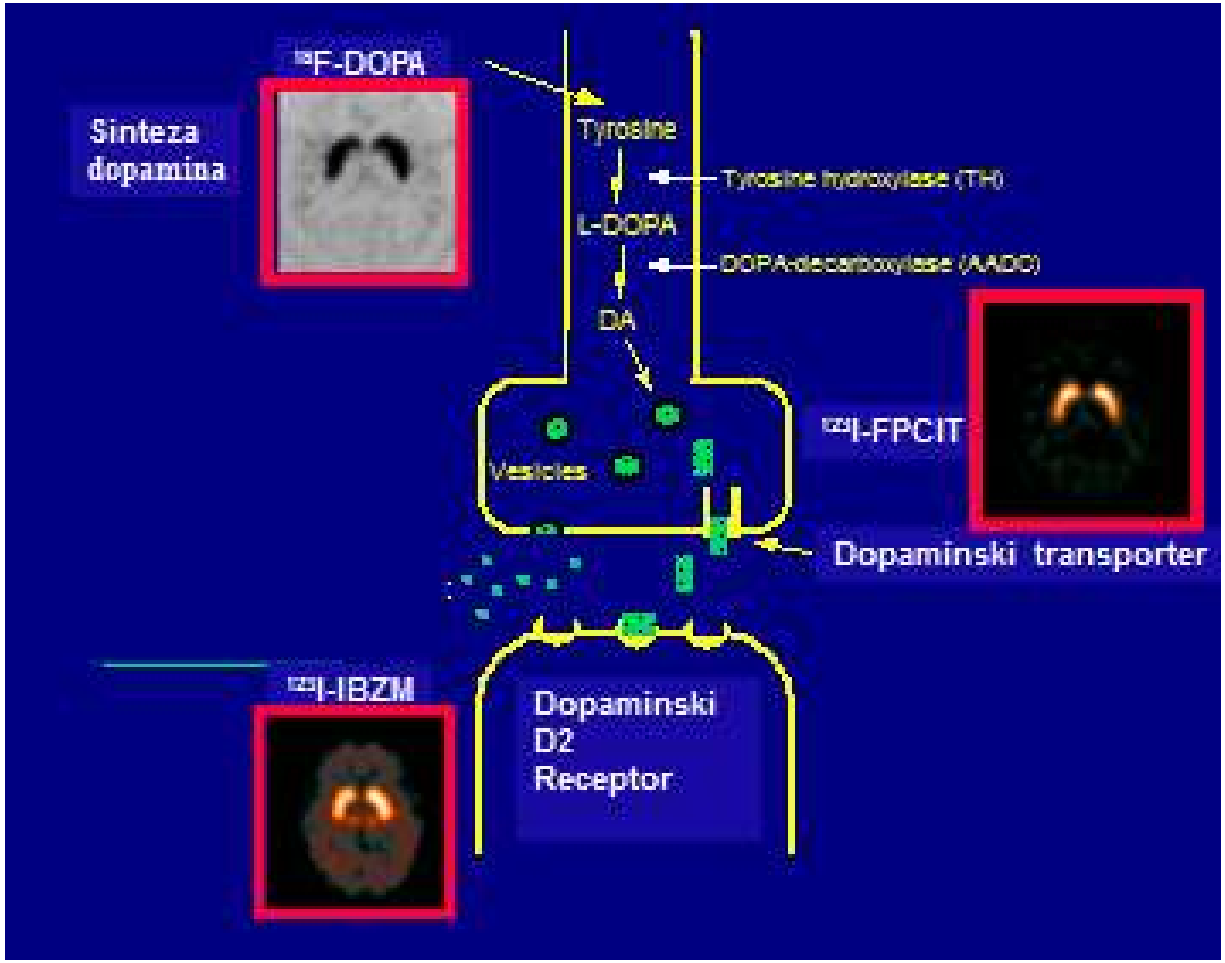
EANM procedure guidelines for brain neurotransmission SPECT using ^{123}I-labelled dopamine transporter ligands, version 2

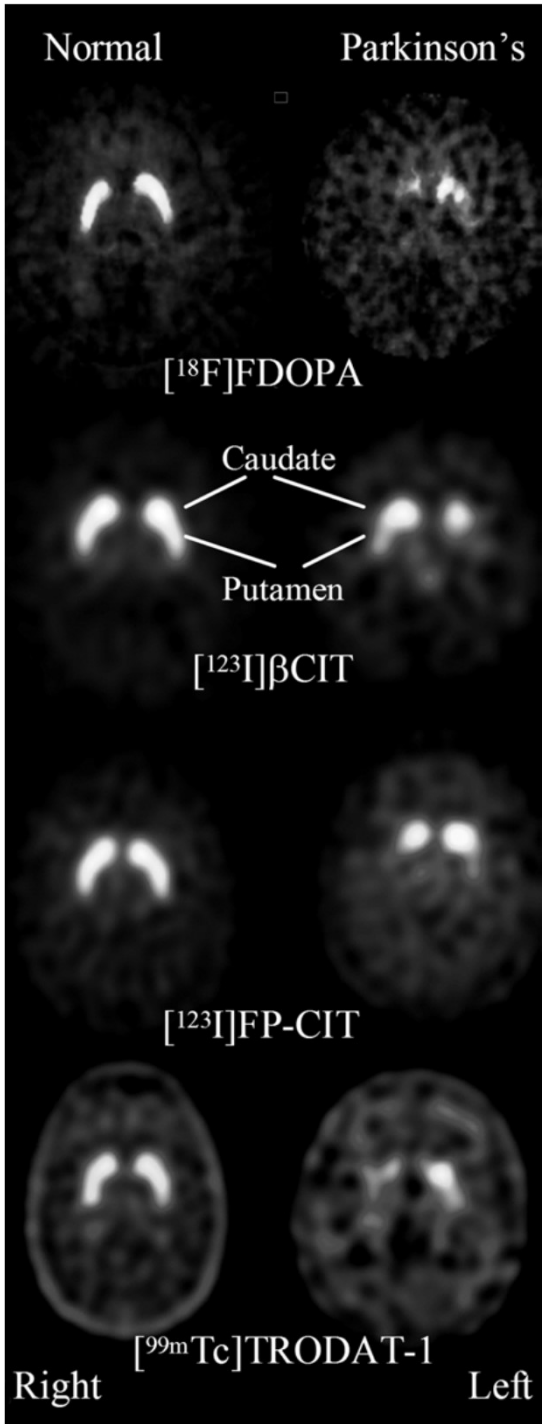
- Various PET tracers have been used to study these presynaptic targets such as ^{18}F-DOPA for the aromatic acid decarboxylase, ^{11}C-DTBZ for VMAT-2 and ^{11}CPE2I for the DAT.
- Various cocaine analogues labelled with ^{123}I suitable for SPECT have shown to bind with high affinity to DAT.
- Currently β-CIT (DOPASCAN) and FP-CIT (DaTSCAN) labeled with I-123
- DAT SPECT
- detecting loss of functional dopaminergic neuron terminals in the striatum of patients with clinically uncertain parkinsonian syndromes. It helps differentiate essential tremor from parkinsonian syndromes related to Parkinson's disease (PD), multiple system atrophy and progressive supranuclear palsy. imaging is indicated for the differentiation of dementia with Lewy bodies from other dementias



	Presynaptic radioligands DOPA decarboxylase (Measures dopamine synthesis)	**SPECT**	**PET** [^{18}F]dopa [^{11}C]dopa
	DAT (Provides measure of functioning dopaminergic terminals)	[^{123}I]FP-CIT [^{123}I]β-CIT [^{99m}Tc]TRODAT-1 [^{123}I]PE2I [^{123}I]-altropane	[^{11}C]cocaine [^{3}H]WIN [^{11}C]altropane [^{11}C]/[^{18}F]β-CFT [^{11}C]FE-CIT [^{11}C]dMP
	VMAT-2 (Marker for dopaminergic terminals)		[^{11}C]DTBZ
	Postsynaptic radioligands D_2 receptor	**SPECT** [^{123}I]IBZM	**PET** [^{11}C]raclopride [^{18}F]DMFP [^{11}C]NMSP

- PET and SPECT radioligands have been developed for imaging of either pre- or post-synaptic components of the dopaminergic system.
- [18F]FDOPA is a PET marker for dopamine synthesis. [18F]FDOPA is converted by the aromatic amino acid decarboxylase (AADC) to [18F]dopamine, which becomes trapped within the presynaptic dopamine neuron.
- The type 2 vesicular monoamine transporter (VMAT2) in the presynaptic dopamine and other monoaminergic neurons pumps newly synthesized or recovered monoamines into the synaptic vesicles. [11C]DTBZ binds to VMAT2 on the presynaptic vesicles containing not only dopamine but also those containing serotonin and histamine). After release into the synapse, excess dopamine is removed from the synapse via reuptake sites (also called dopamine transporters or DAT) located on the presynaptic dopamine nerve terminals.
- Several cocaine- derived radioligands that bind to DAT have been developed for use with both PET and SPECT. Particularly, SPECT DAT radioligands such as [123I] q -CIT, [123I]FP-CIT [123I]altropane and [99mTc]TRODAT-1 have been extensively employed in clinical research.


Sinteza dopamina
^{18}F-DOPA
Tyrosine
Tyrosine hydroxylase (TH)
L-DOPA
DOPA-decarboxylase (AADC)
DA
Vesicles
^{123}I-FPCIT
Dopaminski transporter
^{123}I-IBZM
Dopaminski D2 Receptor


Normal
Parkinson's
[18F]FDOPA
Caudate
Putamen
[123I]βCIT
[123I]FP-CIT
[99mTc]TRODAT-1
Right
Left

Diagnostic Utility of Dopamine PET and SPECT

- Patients with signs and symptoms of parkinsonism (tremor, rigidity, bradykinesia, and postural and gait disturbances) may have PD or any one of a number of other central nervous system disorders such as PSP, MSA, essential tremor, vascular parkinsonism, drug induced parkinsonism and Alzheimer's disease.
- The reductions in striatal radioligand uptake in PD patients have shown two topographic characteristics: radioligand uptake in the striatum contralateral to the clinically more affected side is reduced more compared with the ipsilateral side and radioligand uptake is reduced more in the putamen than in the caudate.
- These findings are consistent with those of pathological studies of PD; degeneration of nigrostriatal neurons usually progresses asymmetrically in two ways; either right or left side is more severely involved and the ventrolateral substantia nigra projecting to putamen degenerates more severely than the ventromedial substantia nigra projecting to caudate.
- Dopamine transporter SPECT may be sensitive enough to detect subclinical involvement of dopamine projections in PD (because 40–50% losses of these projections are said to have occurred before PD patients develop parkinsonian symptoms.

- Dopamine neurons also degenerate in other parkinsonian syndromes such as MSA and PSP. Although the regional asymmetry or unevenness of DAT radioligand or [18F]FDOPA distribution characteristically found in PD is said to be lacking in these parkinsonian syndromes none of the presynaptic imaging techniques can reliably differentiate between these conditions.
- Radioligands allow objective monitoring of disease progression in vivo in patients with PD and other parkinsonian syndromes.

PET and SPECT imaging techniques of neurotransmission systems

- have been shown to be a valuable research tool to further our understanding of the pathophysiological mechanisms of important psychiatric disorders such as schizophrenia, depression and substance abuse.
- imaging the dopamine system, serotonin (5-HT) system,
- dopamine deficiency in the limbic system appears responsible for negative symptoms of schizophrenia
- In major depression, abnormal 5-HT transmission has been linked to its pathophysiology. For the assessment of the serotoninergic system only a few tracers are available, including 11C-ketanserin, 18F-setoperone, 18F-altanserin

	Target site	PET	SPECT
Presynaptic	Synthesis	[^{11}C]methyl-tryptophan	–
	Serotonin transporter	[^{11}C]DASB, [^{11}C]McN 5652	[^{123}I]β-CIT, [^{123}I]ADAM
Postsynaptic	Receptors	–	
	5-HT$_{1A}$	[^{11}C]WAY, [^{18}F]FCWAY	–
	5-HT$_{2A}$	[^{18}F]altanserin	-

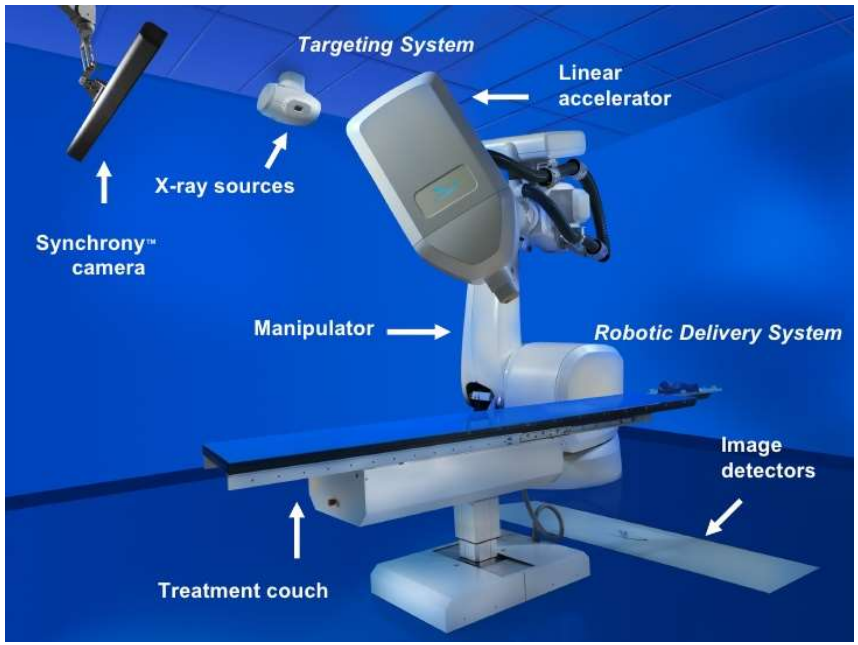
Target site	PET	SPECT
1. Synthesis	[^{18}F]FDOPA	–
2. Dopamine transporter	[^{11}C]cocaine, [^{11}C]methylphenidate, [^{11}C]WIN-35, 428	[^{123}I]β-CIT, [^{123}I]FP-CIT, [^{123}I]altropane,
4. Monoamine transporter	[^{11}C]DTBZ	[^{99m}Tc]TRODAT-1
3. Receptors	–	–
D_1	[^{11}C]SCH 23390, [^{11}C]NNC 112	–
D_2	[^{11}C]raclopride, [^{11}C]FLB 457, [^{18}F]fallypride	[^{123}I]IBZM, [^{123}I]IBF, [^{123}I]epidepride

- in patients with major depressive disorder decreased perfusion is associated specifically with negative symptom severity.
- PET and SPECT imaging of neuroreceptors and transporters has been used to study antipsychotic or antidepressant drug action by examining the relationship between neuroreceptor or transporter occupancy of psychiatric drugs and clinical response
- 11C-L-deprenyl can be used to measure the effect of therapy in patients under treatment with MAO-B inhibitors
- autistic children underwent Tc-99m-HMPAO brain SPECT scans, which showed significant decreases in rCBF to the temporal lobes and frontal lobes. The corresponding CT and MRI scans failed to show any abnormality.

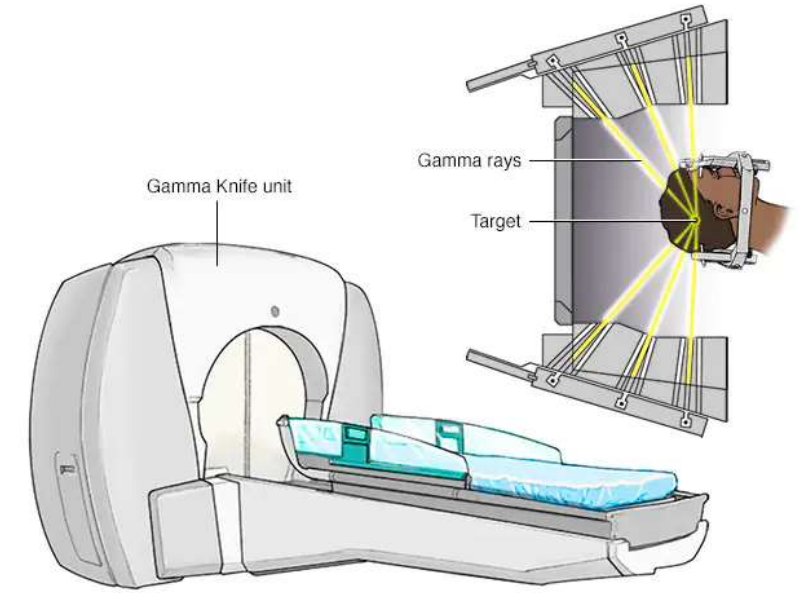
Gamma Knife Radiosurgery

- This type of radiation treatment is usually performed when:
- A tumor or other difference in the brain is too hard to reach with standard neurosurgery.
- A person isn't healthy enough for standard surgery.
- Gamma Knife radiosurgery is most commonly used to treat the following conditions:
- Tumors (83% GK radiosurgery): radiosurgery or microscopic resection, is preferable for a patient with a relatively small tumor (<3cm)
- glial tumors have been undergoing this treatment in recent years
- Benign : acoustic neuroma (vestibular schwannoma), pituitary tumors, meningiomas
- Brain metastases:The successful use of GK radiosurgery to treat brain metastasis, a recurrent hypernephroma, was first reported in 1989. GK radiosurgery has since been used as a primary or booster, with whole brain radiation therapy (WBRT), treatment for increasing numbers of metastatic cancer patients. This technique is particularly suitable because many metastatic lesions are well circumscribed.For single metastases, stereotactic radiosurgery, with or without WBRT, achieves results comparable to those of conventional surgery combined with WBRT.
- Arteriovenous malformation (AVM) 12-15 %. AVMs, if not treated, may "steal" the typical flow of blood from the brain. This can cause a stroke or lead to bleeding in the brain.
- Trigeminal neuralgia.

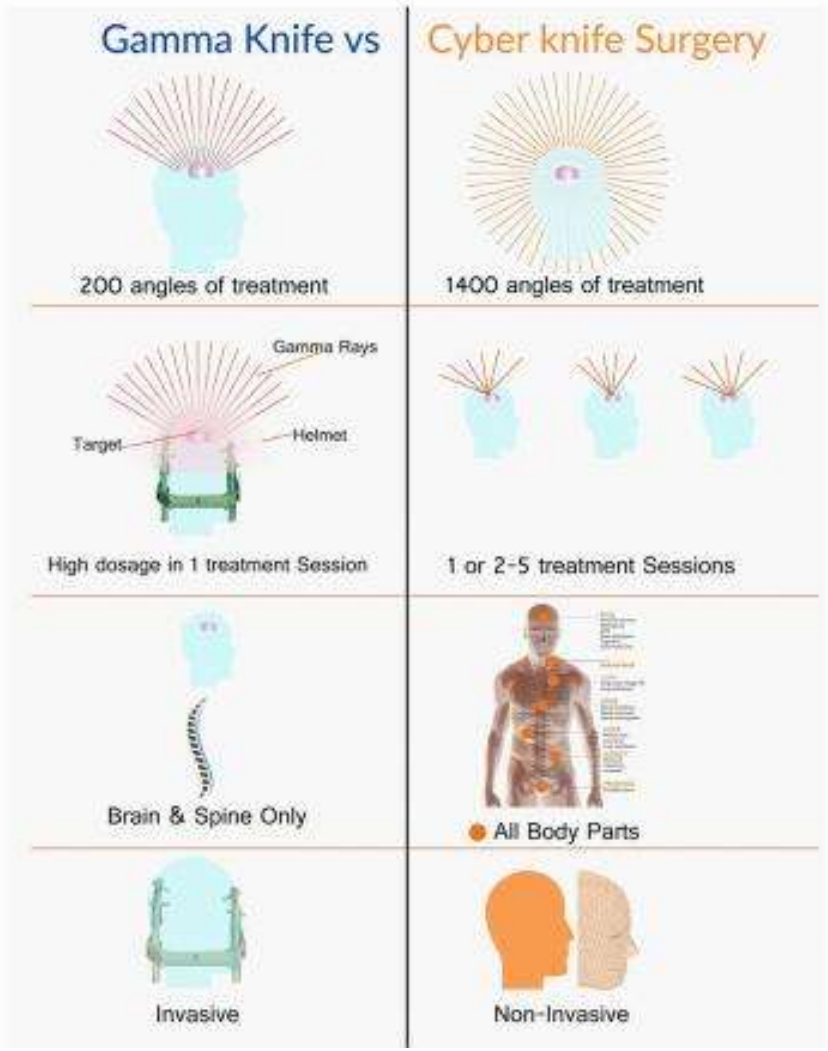
CyberKnife



Gamma Knife



Gamma Knife vs. CyberKnife



Difference Between Gamma Knife and CyberKnife

- CyberKnife is an innovative frameless radiosurgical system that provides precise target lineation without the need for a rigid stereotactic frame for immobilization. Additionally, in contrast to the frame-based Gamma Knife method, the high-dose treatments with CyberKnife could be divided into more fractions to control tissue dose, thereby reducing toxicity from treatment.
- Both Gamma Knife and CyberKnife are the dominant methods of stereotactic radiosurgery (SRS) used to treat malignant brain tumors and other functional abnormalities in the brain. However, Gamma Knife is a frame-based radiosurgery technique that requires the application of an invasive frame to the patient's head to achieve the desired accuracy. CyberKnife, on the contrary, uses a robotic arm to deliver radiation beams to the targeted tumor from multiple positions and angles in order to destroy the tumor cells.
- Gamma Knife is a non-invasive stereotactic radiosurgery procedure that uses intense beams of gamma rays with pinpoint accuracy to treat functional abnormalities in the brain. Despite the name, it involves no incision, not even a knife; a large metal frame – the collimator – pierced by hundreds of holes is mounted onto the patient's head and a single, radiation dose is administered throughout the target volume using multiple exposures.

Gamma Knife	CyberKnife
It is a frame-based radiosurgery technique that requires the application of an invasive frame to the patient's head to achieve the desired accuracy.	It is a frameless radiosurgical system that provides precise target lineation without the need for a rigid stereotactic frame for immobilization.
It employs cobalt radiation sources in a fixed hemispherical array, such that all photon beams focus on a single point.	They deliver their radiation beams one at a time instead of delivering radiation into convenient primitive shapes for precise target delineation.
It uses intense beams of gamma rays with pinpoint accuracy to treat functional abnormalities in the brain.	It uses a robotic arm to deliver radiation beams to the targeted tumor from multiple positions and angles to destroy tumor cells.
It is designed to target tumors within the skull or cervical spine tumors.	It can treat tumor cells from multiple angles anywhere in the body.
The head frame is required for sub-millimeter accuracy.	The head frame is not required for sub-millimeter accuracy.