PET-CT in Brain Tumors

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Classification of brain tumors

Topographically –

- Supratentorial
- Infratentorial
- Posterior fossa tumours
- Intermediate (straddling tentorial notch or foramen magnum)

WHO Classification : MC, based on supposed "cell of origin"

WHO classification

Astrocytic tumors

- Pilocytic astrocytoma (WHO grade I)
- Diffuse Astrocytoma (WHO grade II)
- Anaplastic (malignant) astrocytoma (WHO grade III)
- Glioblastoma multiforme (WHO grade IV)
- Subependymal giant cell astrocytoma (WHO grade I)
- Pleomorphic xanthoastrocytoma (WHO graade II/ III)

Oligodendroglial tumors

- Oligodendroglioma (WHO grade II)
- Anaplastic oligodendroglioma (WHO grade III)

Ependymal cell tumors

- Subependymoma (WHO grade I)
- Ependymoma (WHO grade II)
- Anaplastic ependymoma (WHO grade III)

Mixed gliomas

- Mixed oligoastrocytoma (WHO grade II)
- Anaplastic (malignant) oligoastrocytoma (WHO grade III)
- Others (*e.g.* ependymo-astrocytomas)

Neuroepithelial tumors of uncertain origin

- Polar spongioblastoma (WHO grade IV)
- Astroblastoma (WHO grade IV)
- Gliomatosis cerebri (WHO grade IV)

Tumors of the choroid plexus

- Choroid plexus papilloma
- Choroid plexus carcinoma (anaplastic choroid plexus papilloma)

Pineal Parenchyma Tumors

- Pineocytoma
- Pineoblastoma
- Mixed pineocytoma/pineoblastoma

Neuronal and mixed neuronal-glial tumors

- Gangliocytoma
- Dysplastic gangliocytoma of cerebellum
- Ganglioglioma
- Anaplastic ganglioglioma
- Desmoplastic infantile ganglioglioma
- Central neurocytoma
- Dysembryoplastic neuroepithelial tumor
- Olfactory neuroblastoma (esthesioneuroblastoma)

Tumors with neuroblastic or glioblastic elements

- Medulloepithelioma
- PNET with multipotent differentiation
- Neuroblastoma
- Retinoblastoma
- Ependymoblastoma

Tumors of cranial nerves

Schwannoma , neurofibroma

Tumors of meninges

– meningioma, hemangiopericytoma, hemangioblastoma

Tumors of hematopoietic

– primary and secondary CNS lymphoma

Germ cell

– germinoma , teratoma

Tumors of sella

– pitutary adenoma, craniopharyngioma, rathke cleft cyst, chordoma

Metastatic tumors

Intracranial tumours

A. < 15 yrs

- CNS tumours 2nd most common cancer (Leukemia MC)
- 50- 70% Paediatric brain tumours are infratentorial
- < 2 yrs of age, 2/3rd are supra tentorial
- Metastases are rare.

B. > 15 yrs

-Supratentorial – 70%

-Metastases are common.

CNS Tumors in Pediatric Age Group

SUPRATENTORIAL (50%)

- Covering of brain: dural sarcoma, schwannoma, meningioma (3%)
- Cerebral hemisphere: astrocytoma (37%), oligodendroglioma
- Corpus callosum: astrocytoma
- 3rd ventricle: colloid cyst, ependymoma
- Lateral ventricle: ependymoma (5%), choroid plexus papilloma (12%)
- Optic chiasma: craniopharyngioma (12%), optic nerve glioma (13%), teratoma, pituitary adenoma
- Hypothalamus: glioma (8%), hamartoma
- Pineal region: germinoma, pinealoma, teratoma

- **INFRATENTORIAL (50%)**
  - **B**rainstem glioma
  - **E**pendymoma (4th ventricle)
  - **M**edulloblastoma (Cerebellum)
  - **A**strocytoma (Cerebellum)
  - **C**horoid plexus papilloma (4th ventricle)
  - **H**emangioblastoma

Astrocytomas

Low-grade astrocytoma (benign astrocytoma)

- Incidence: 25 – 30 % of astrocytoma
- Age : younger age group
- Location: white matter
- Pathology:
  - no necrosis
  - no vascularity; haemorrhage rare
  - oedema uncommon,
  - may be either focal / diffusely infiltrating,
  - calcification in 15 – 20% of patients
- Survival: 3 – 10 yrs

Cont.....

- **Radiologically:**
  - Sharply marginated, well delineated,
  - Oedema – rare
  - Cyst formation – common, with mural nodule,
  - Calcification occasionally.

- **CT:** Isodense or hypodense, with marked enhancement of nodule.

- **MRI:** - Isointense or hypointense on T1WI,
  - hyperintense on T2WI: enhancement of nodule but not the cyst wall

Anaplastic astrocytoma

- Incidence: 25 – 30 % of astrocytoma.
- Age: greater than 40 years.
- Location: proportional to white matter.
- Pathology: more hyper cellularity & pleomorphism, mitosis & endothelial proliferation common, necrosis absent.
- Radiologically: compared to benign astrocytoma

  Less well defined, more mass effect, more contrast enhancement, more heterogenecity on both CT & MRI, less commonly calcified.

Glioblastoma multiforme.[GBM]

- **Incidence:** 50 % of Astrocytoma
- **Age:** 5^{th} – 7^{th} decades. [age at diagnosis is single most powerful predictor of histologic findings and survival. In general older the patient, the more malignant the astrocytoma and the worse the prognosis.]
- **Location:** supratentorial cerebral hemispheres
- **Pathology:** necrosis and hemorrhage.
- **Radiologically:**

  Compared with benign astrocytoma, greater mass effect, vasogenic edema, heterogeneity, and enhancement.

- Investigation of choice/gold standard is MRI

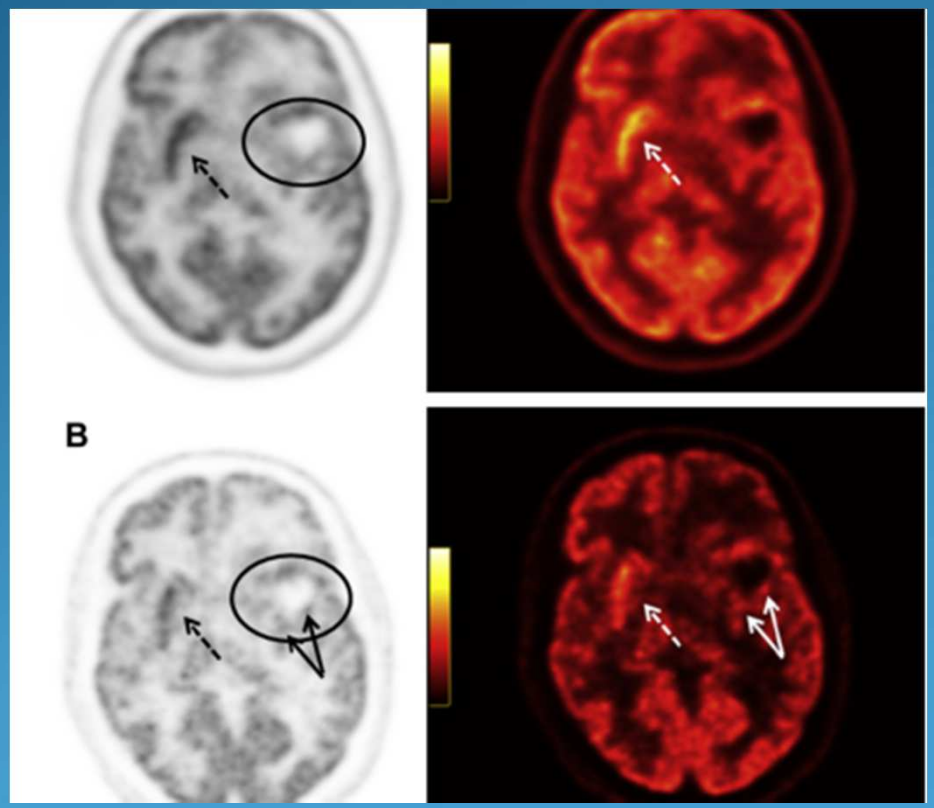
18F-Fluorodeoxyglucose PET-CT

- Primary brain tumors have increased glucose metabolism and uptake.
- FDG is actively transported across the intact BBB, hence it can complement structural imgaing by giving valuable functional data on tumor biology.

- Tumor grading
- Stereotactic biopsy guidance
- Prognostication
- Evaluation of completeness of tumor surgery
- Tumor recurrence versus RT changes
- Chemotherapy response assessment
- Radiotherapy planning

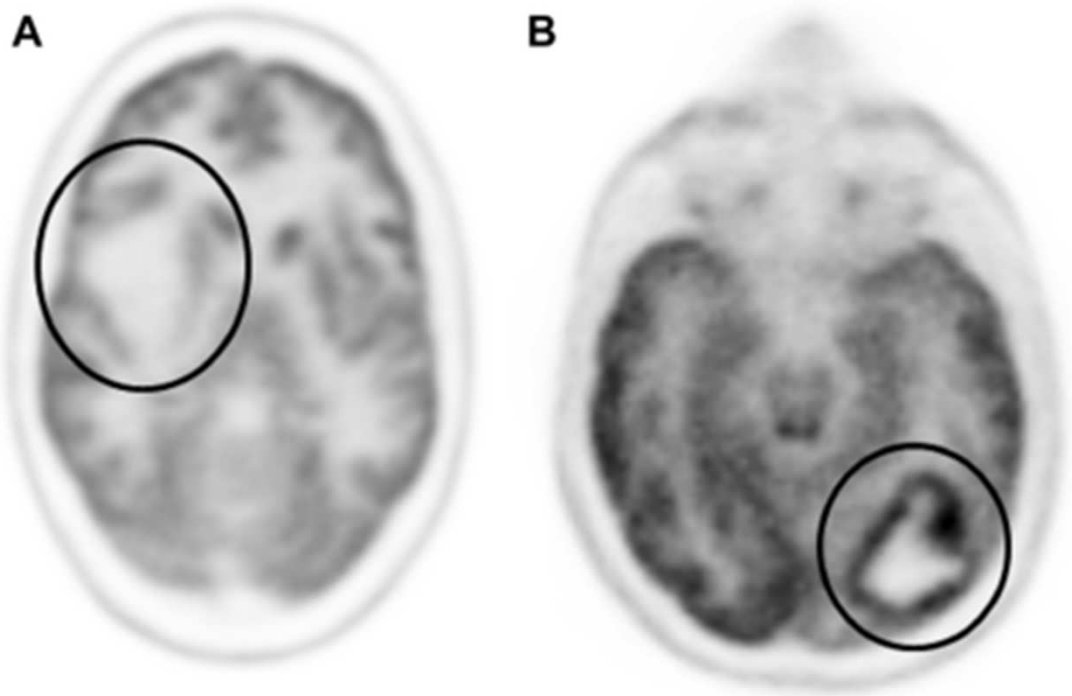
Initial evaluation of primary tumors

- MRI is the investigation of choice



01 hr and 03 hr delayed images revealing increased wash out and better tumor to background ratio

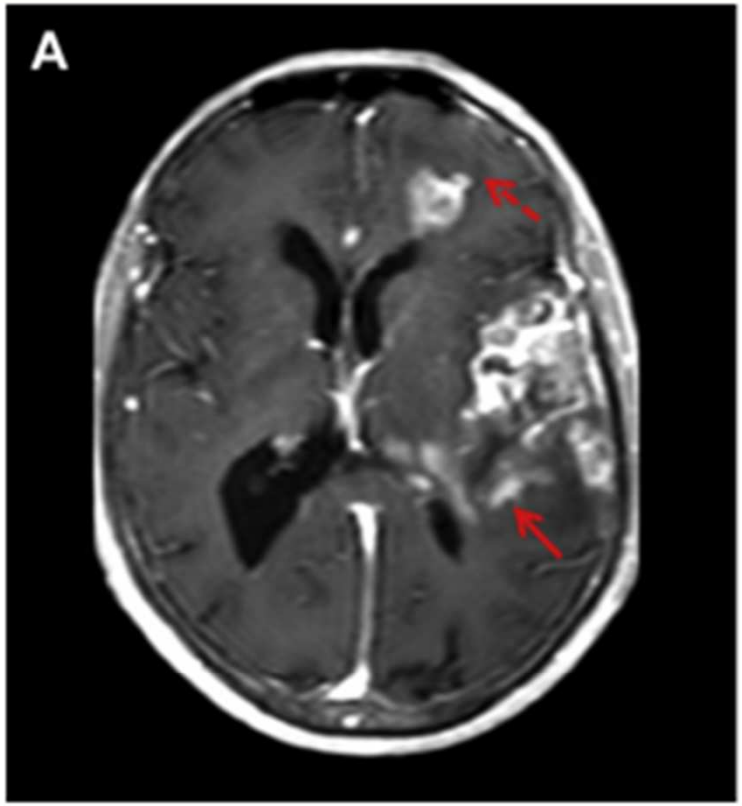
Tumor grade determination

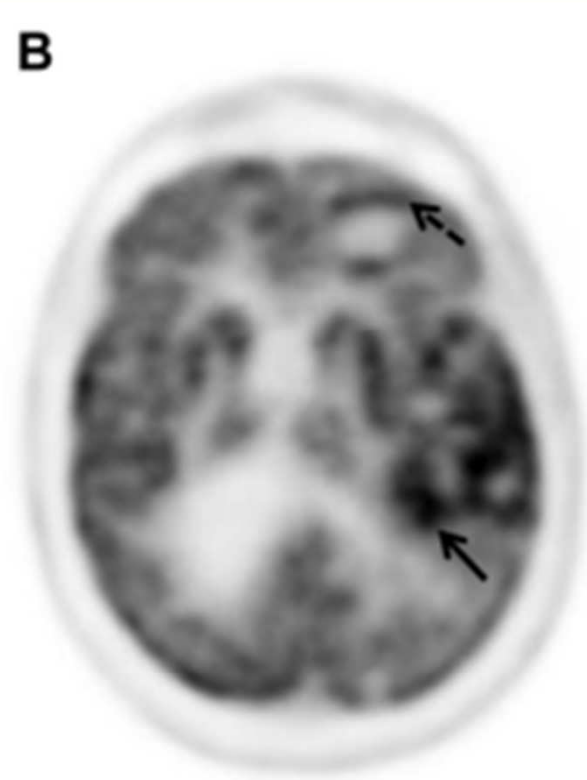


[redacted]. Example of different metabolism in different tumors. FDG-PET of an MR and biopsy-verified low-grade glioma (*A*) and high-grade glioma (*B*) at the time of diagnosis.

Sterotactic biopsy guidance

- Gliomas show cellular heterogenity.
- This is at times unidentified on structural imaging.
- PET identifies areas with highest metabolism for guidance for stereotactic biopsy.





Example of the use of FDG-PET/CT as guidance for stereotactic biopsy. Transaxial MR image (*A*) shows contrast enhancement in lesion area (*red dashed and solid arrows*), whereas PET images (*B*) provide additional information in the shape of high avidity, and hence malignancy, in the edge of a solid frontal tumor (*black dashed arrow*) and in a heterogeneous temporal lesion (*solid black arrow*).

Prognostication

- FDG uptake can give additional information on tumor aggressiveness and can act as an adjunct to conventional prognostication markers.

Tumor recurrence versus radiation necrosis

- Challenging on MR
- FDG-PET seems to be a valuable clinical tool. Suspicious lesions on MR imaging that show increased FDG uptake (ie, uptake equal to or great than that in normal cortex) are likely to represent tumor recurrence.
- Sensitivity is an issue, especially but not exclusively with low-grade gliomas. Although false-positive results may occur, specificity is usually high in routine clinical practice.

RT Planning

- Structural imaging is usually applied to delineate target volumes, but PET may offer better target definitions by adding biological/metabolic information to the conventional anatomic gross target volumes and clinical target volumes.
- Some tumor areas are more metabolically active but not readily appreciated structurally, which may lead to insufficient treatment and poorer outcome.

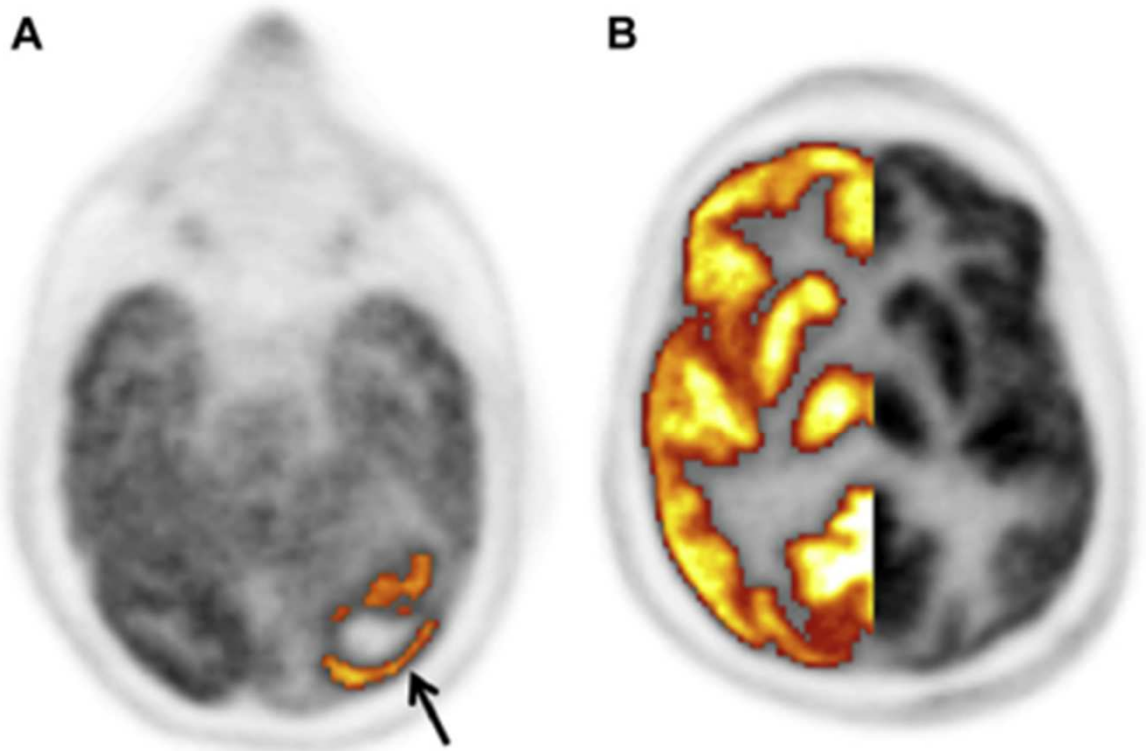
RT planning

- Also, recurrence is most likely to occur near the original tumor site. FDG-PET may identify hot spots with higher cell density suggestive of residual tumor tissue, and thereby assist in maximizing the radiation effect with the least collateral dam

Changes of management with FDG

- A recent publication based on the National Oncologic PET Registry (NOPR) examined retrospectively data from 479 patients with primary brain tumors (72%) or brain metastasis (28%) and found that overall, FDG-PET imaging changed the intended management in 38% of patients with primary brain tumors.

Novel softwares

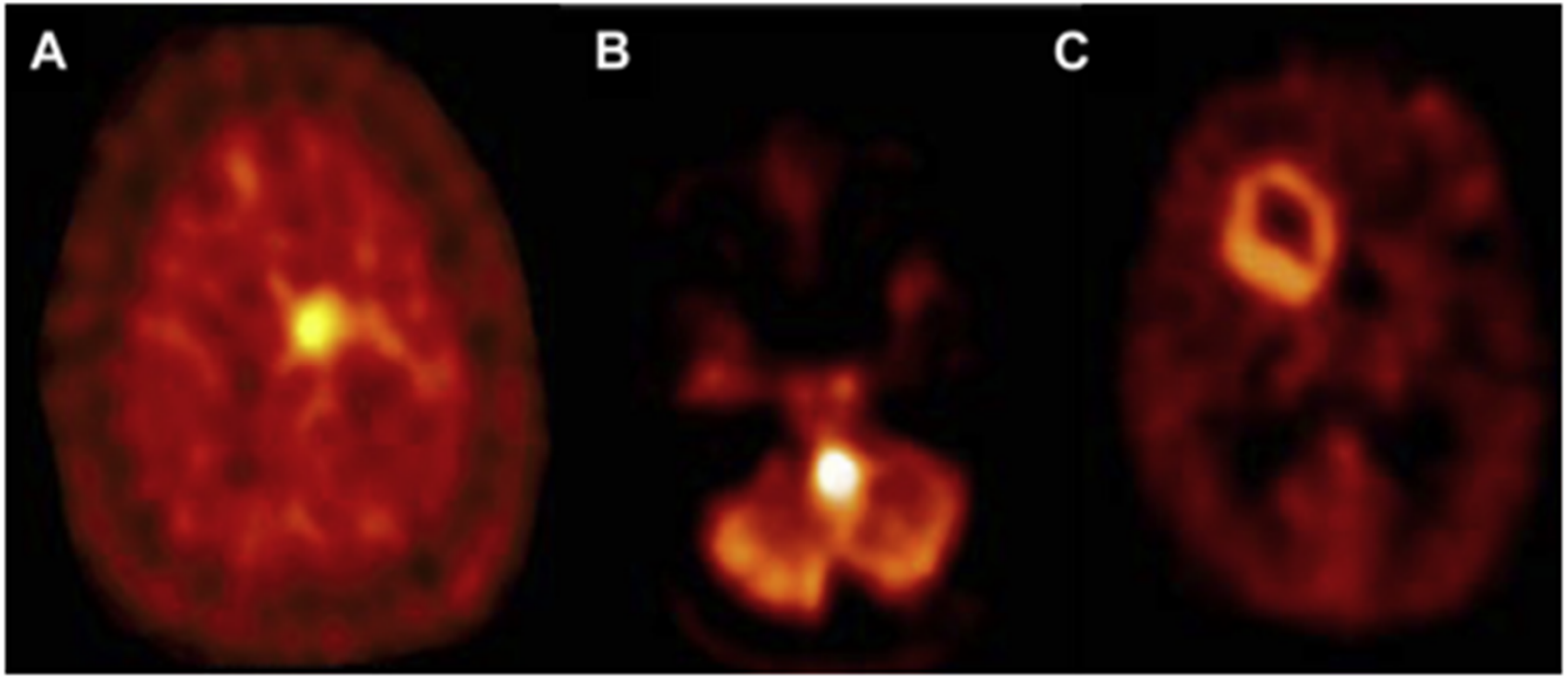


[redacted]. Example of segmentation with the novel software ROVER. Transaxial images show regions of interest (*arrow*) generated by 3-dimensional spheres of tumor (*A*) and right hemisphere (*B*). ROVER automatically corrects for partial volume effects.

18F DOPA PET-CT

- Increased amino acid metabolism in brain and no uptake in the normal brain parenchyma, gives greater contrast.

11C Methionine



^{11}C-Methionine uptake in a low-grade glioma (*A*), grade III astrocytoma (*B*), and glioblastoma multiforme (*C*).

False positive

- Demyelination
- Leukoencephalitis
- Abscess

18F-FLT

- DNA proliferation index

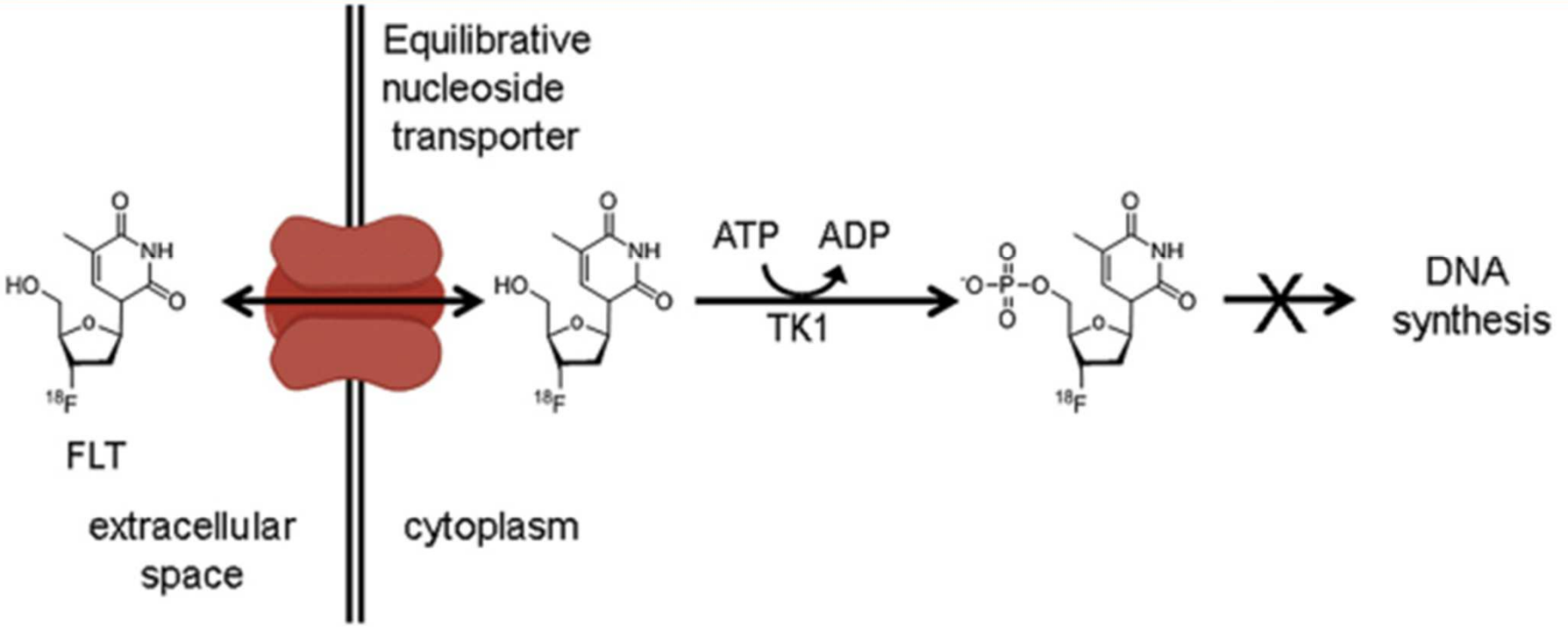
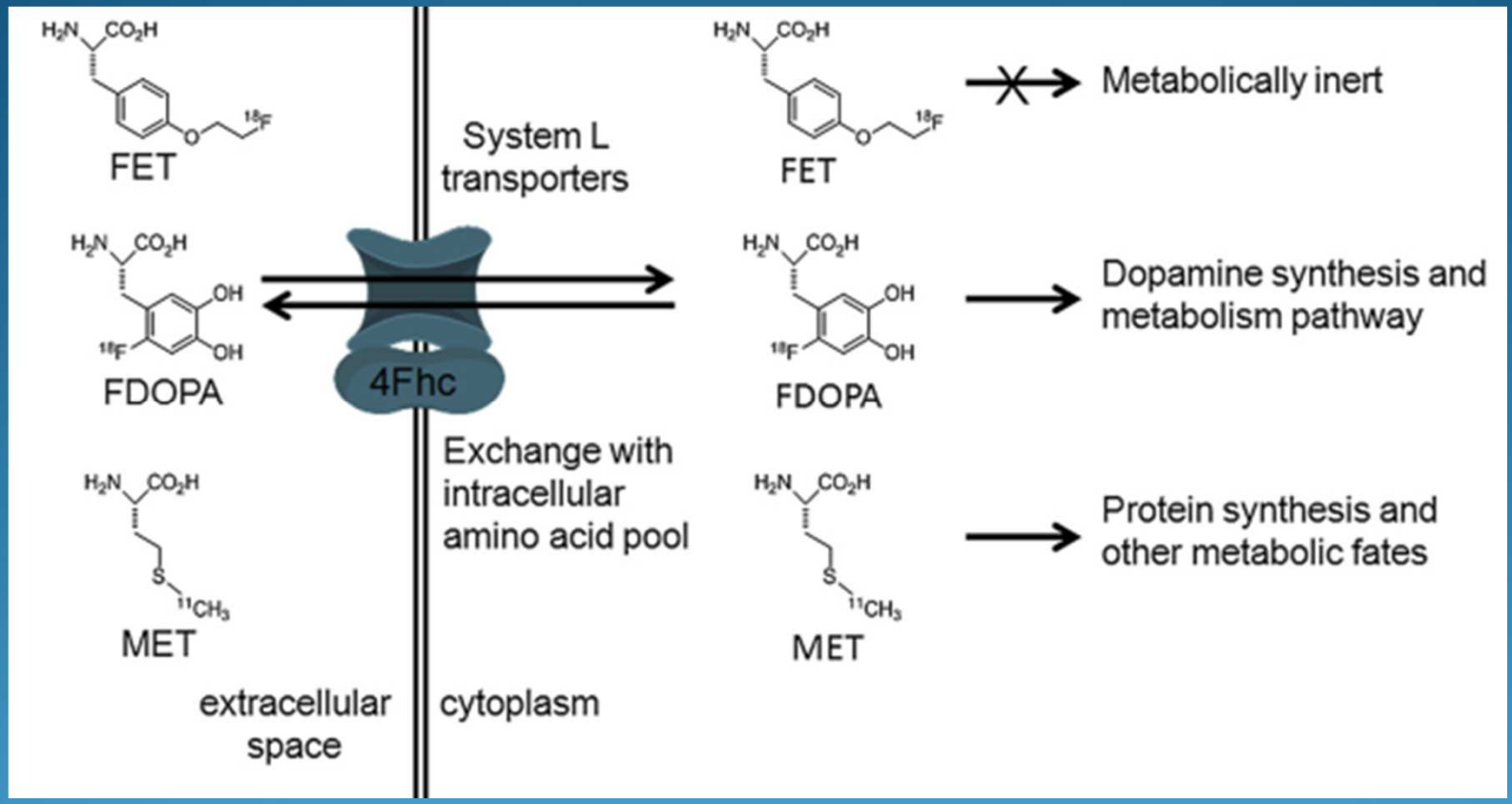


Fig. 2. Cellular uptake and trapping of ^{18}F-FLT. ^{18}F-FLT enters cells through a combination of diffusion and transport by the equilibrative nucleoside transporter 1 (ENT-1). Phosphorylation of ^{18}F-FLT is mediated by thymidine kinase 1 (TK1) and traps ^{18}F-FLT-5-phosphate within the cell, which cannot participate in DNA synthesis.

Radiolabelled amino acids

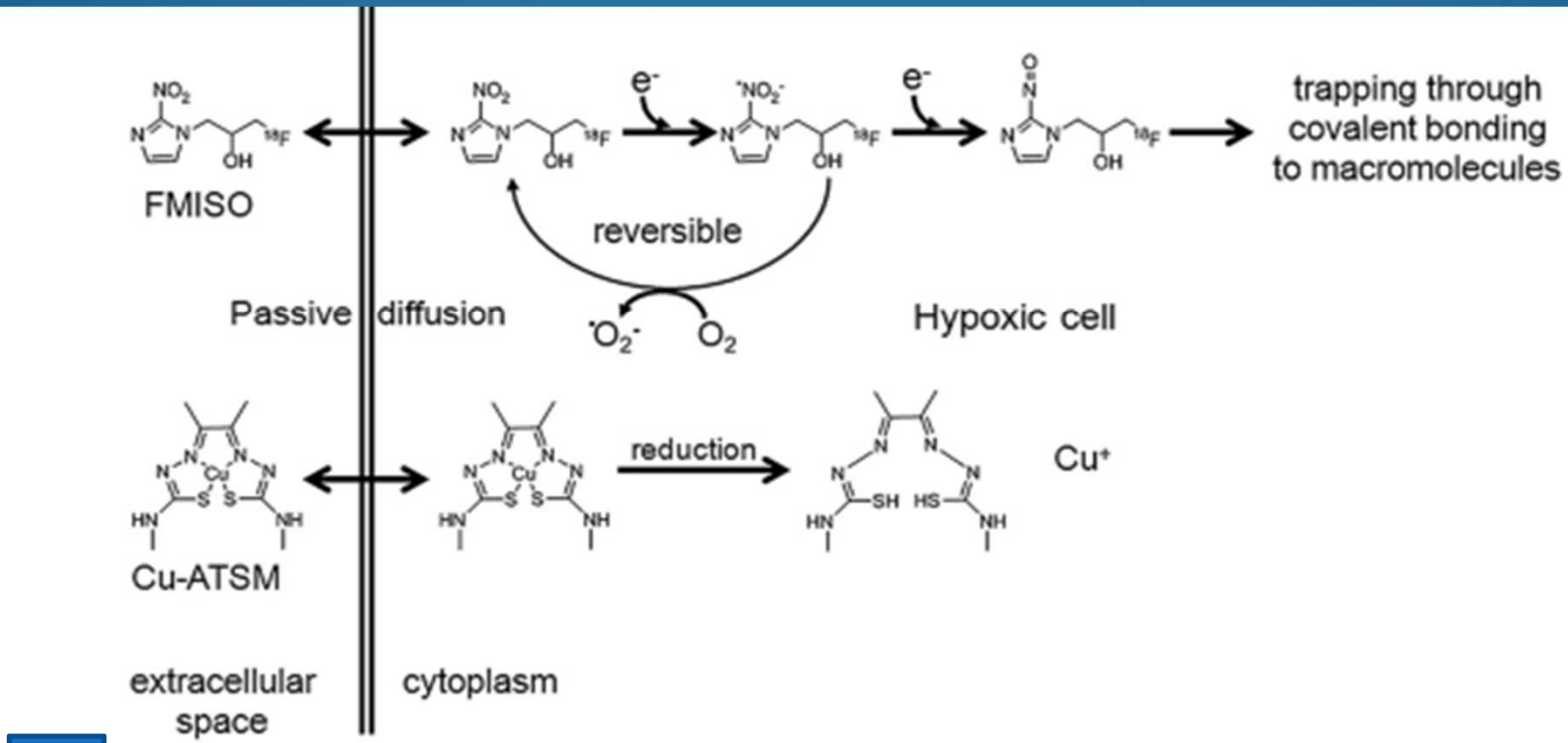


. Cellular uptake of the system AA transporter substrates ^{18}F-FET, ^{18}F-FDOPA, and ^{11}C-MET. System L substrates cross the BBB and enter cells through system L transporters that can mediate both AA uptake and efflux. Transport via LAT1 and LAT2 requires heterodimerization with the heavy-chain glycoprotein 4FHc (SLC3A2), and the mechanism of transport involves the exchange of an extracellular AA substrate with an intracellular AA. LAT3 and LAT4 mediate facilitated diffusion and do not require 4FHc. Once inside the cell, ^{18}F-FDOPA and ^{11}C-MET undergo further metabolism while ^{18}F-FET does not.

Radiolabelled amino acids.

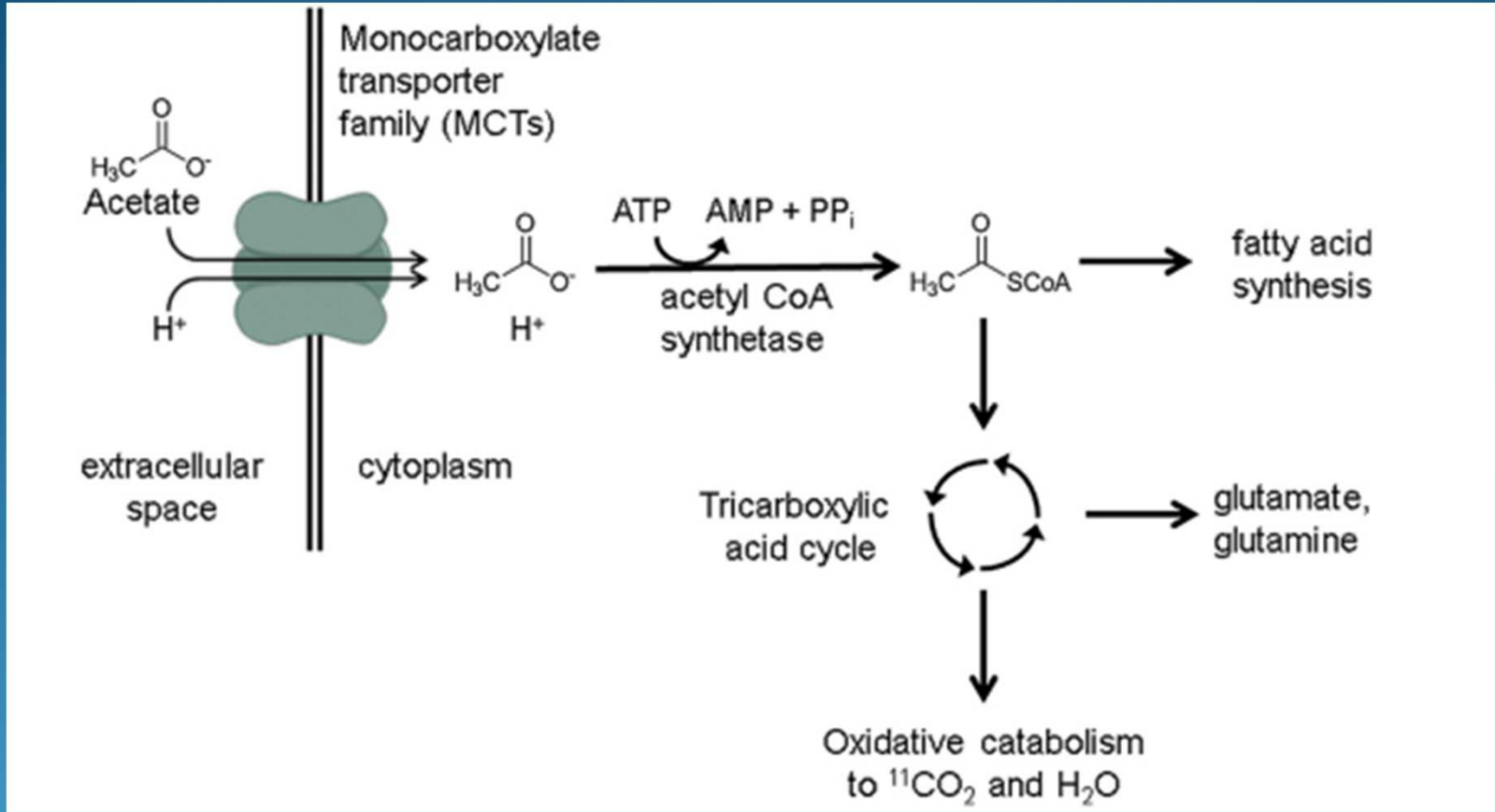
- Superior to 18F-FDG PET/CT in imaging brain gliomas

Hypoxia imaging agents



Cellular uptake and trapping of ^{18}F-FMISO and Cu-ATSM. The hypoxia-sensitive tracers ^{18}F-FMISO and Cu-ATSM cross the BBB and enter cells via passive diffusion. In hypoxic cells, both tracers are reduced, which leads to retention inside cells through reaction with macromolecules in the case of ^{18}F-FMISO and loss of copper in the case of Cu-ATSM.

11C Acetate PET



Cellular uptake and metabolism of ^{11}C-ACE. ^{11}C-ACE crosses the BBB and enters cells through the monocarboxylate transporter (MCT) family including MCT1, MCT2, and MCT4. Within cells, ^{11}C-ACE can undergo oxidative catabolism to produce energy through the tricarboxylic acid (TCA) cycle, or alternatively be incorporated into fatty acids in the cell membranes. In normal brain as well as gliomas and meningiomas, TCA-cycle intermediates derived from ^{11}C-ACE may be converted into AAs, for example, glutamine and glutamate as well as other metabolic intermediates. AMP, adenosine monophosphate; PP_i, inorganic pyrophosphate.


L BENCH PET
BIODEX

Thank you


Positron Emission Tomography (64 Slice CT)