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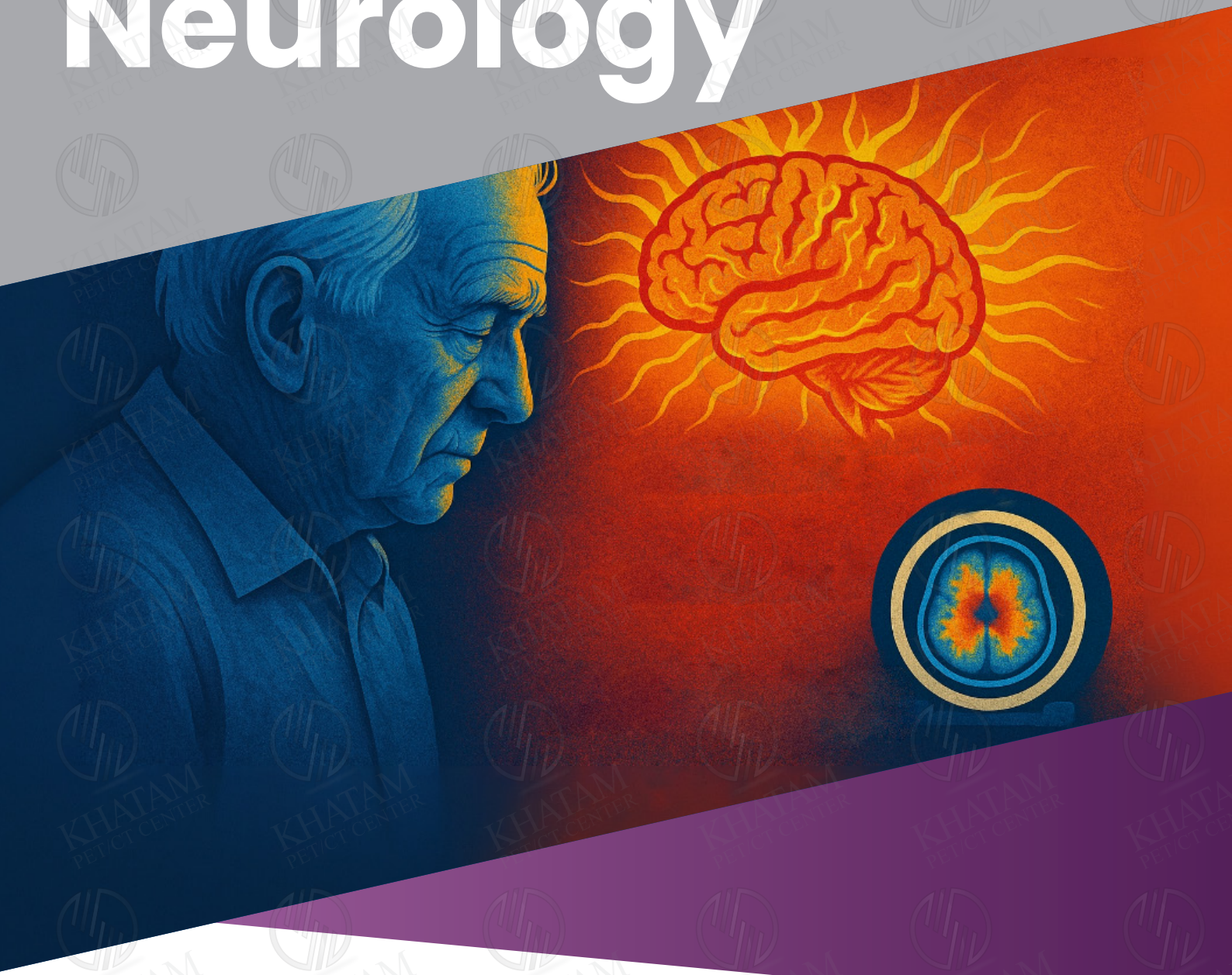
PET/CT in Neurology



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Introduction

Positron emission tomography-computed tomography (PET/CT) is a vital imaging technique in neurology, particularly for diagnosing and managing neurological disorders. This hybrid imaging modality assesses metabolic processes in the brain, providing crucial insights into conditions such as epilepsy, dementia, and cerebrovascular diseases.

Some advantages of PET/CT in neurology:

- Combines functional and anatomical imaging.
- Provides quantitative data on metabolic activity.
- Helps in early diagnosis and differential diagnosis of complex neurological conditions.

Common tracers used in neurological PET/CT:

- ^{18}F-fluorodeoxyglucose (FDG): Measures glucose metabolism.
- Amyloid Tracers: Detect amyloid plaques (e.g., florbetapir, florbetaben).
- Tau Tracers: Detect tau pathology (e.g., flortaucipir).
- Amino Acid Tracers: Assess tumor metabolism (e.g., ^{18}F-FET, 11C-MET).

Here, we summarize the latest guidelines and recommendations on PET/CT applications in neurology:

Neurodegenerative Diseases:

PET/CT imaging is an invaluable tool in dementia diagnosis and management. Its ability to differentiate between different types of dementia, predict disease progression, and monitor treatment efficacy makes it essential for clinicians aiming to provide tailored interventions and improve patient outcomes.

Importance of PET/CT in Dementia:

- Differentiation of Different Dementia Types:

PET/CT scans are particularly effective in distinguishing between different types of dementia, such as Alzheimer's disease (AD), frontotemporal dementia (FTD), and dementia with Lewy bodies (DLB). For instance, reduced glucose metabolism in specific brain regions, like the temporal and parietal lobes, indicates AD, while distinct patterns are observed in FTD and DLB. This differentiation is critical for appropriate treatment planning and management.

- Early Diagnosis and Predictive Value:

^{18}F-FDG PET imaging allows for detecting early metabolic changes associated with neurodegenerative disorders before structural changes become apparent on CT or MRI. This capability is particularly beneficial in patients with mild cognitive impairment (MCI), where specific metabolic reductions can predict the progression to dementia.

- Monitoring Treatment Efficacy:

PET/CT not only aids in diagnosis but also serves as a tool for monitoring the effectiveness of disease-modifying therapies (DMTs). Regular imaging can track changes in amyloid burden and brain metabolism, enabling clinicians to adjust treatment plans accordingly.

Alzheimer's disease (AD)

AD is the leading cause of dementia, with its diagnosis and management remaining challenging. Amyloid PET has become increasingly important in medical practice for patients with AD.

Diagnostic Use of PET/CT in AD

1- Glucose Metabolism (FDG-PET):

Alzheimer's typically shows reduced glucose metabolism in the temporoparietal and posterior cingulate regions, helping differentiate it from other dementias (e.g., frontotemporal dementia).

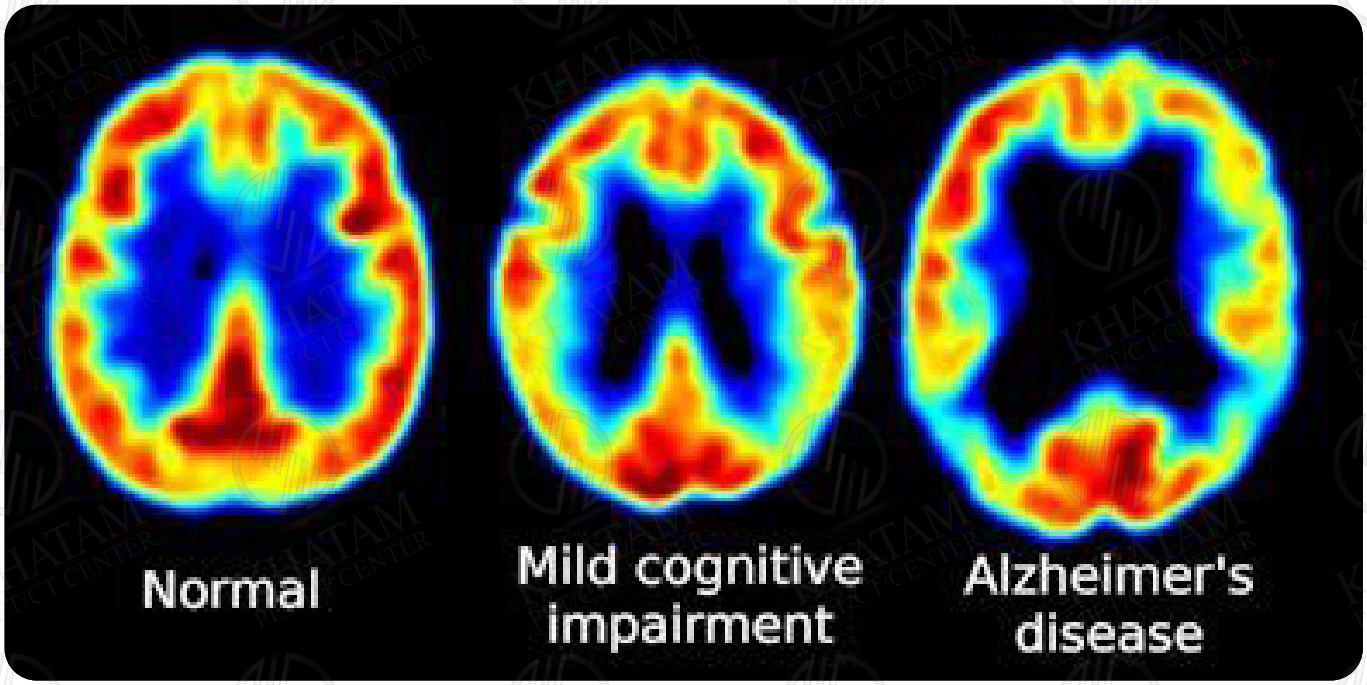

Figure 1. ^{18}F-FDG PET images show reduced glucose metabolism in temporal and parietal regions in patients with MCI and Alzheimer's

2- Amyloid Imaging:

PET/CT can detect amyloid-beta plaques, a hallmark of Alzheimer's disease, using radiotracers like florbetapir, florbetaben, and flutemetamol.

Amyloid PET (^{18}F-florbetapir) indications:

- Persistent or progressive unexplained MCI (Mild Cognitive Impairment)
- Patients satisfying core clinical criteria for possible Alzheimer's disease (atypical clinical course or etiologically mixed presentation)
- Atypically young-onset dementia
- Differentiating AD from frontotemporal dementia
- Predicting chance of progression to AD in patients with MCI (70% in patients with positive amyloid scan)

3- Tau Imaging:

- Purpose: Detects tau protein tangles, another key feature of Alzheimer's disease.
- Tracers: Tracers like flortaucipir bind to tau aggregates.
- Use: Helps assessing the progression of Alzheimer's, as tau pathology correlates more closely with cognitive decline than amyloid.

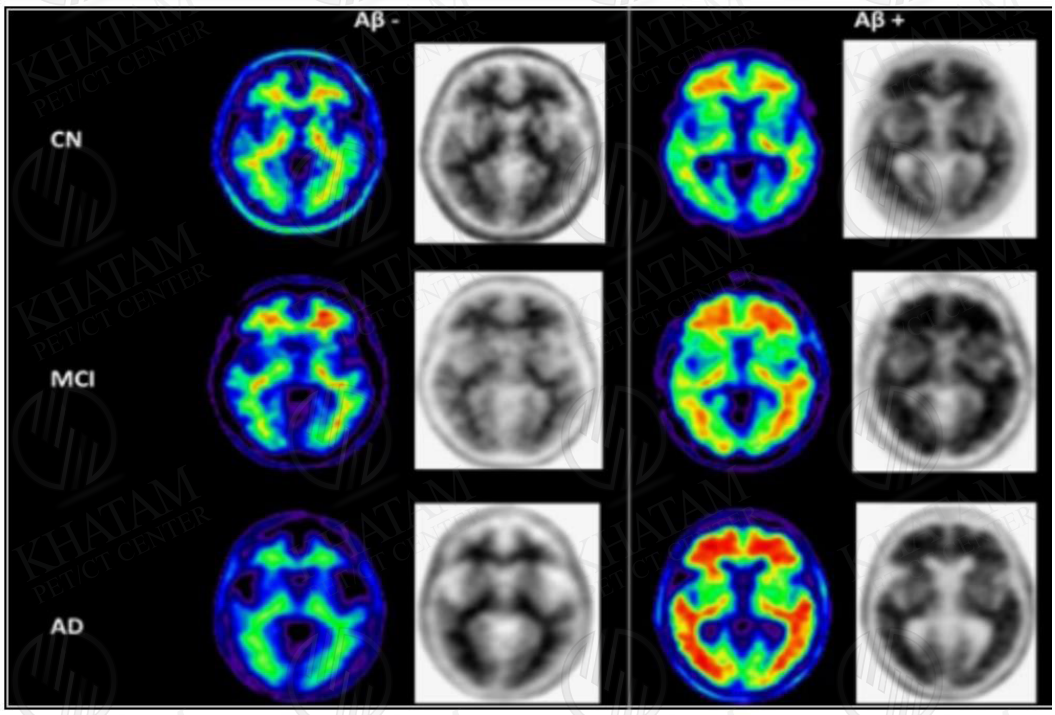

Figure 2. Example images of Aβ- and Aβ+ subjects clinically classified as cognitively normal (CN), MCI, and AD. Note the absence of gray matter uptake and the difference in average cortical SUVR (standard uptake values relative to the cerebellum) in the Aβ- vs Aβ+ classified scans.

Frontotemporal Dementia (FTD)

FTD is a group of neurodegenerative disorders characterized by progressive nerve cell loss in the brain's frontal or temporal lobes. It presents with a variety of symptoms, including changes in personality, behavior, and language, which can overlap with other neurodegenerative and psychiatric disorders. PET/CT plays a significant role in diagnosing and differentiating FTD from other dementias.

Diagnostic Use of PET/CT in FTD

1- ^{18}F-FDG PET/CT:

In FTD, hypometabolism is typically observed in the frontal and/or anterior temporal regions, while Alzheimer's disease often shows hypometabolism in the parietal and temporal lobes, particularly the posterior cingulate cortex. Asymmetrical patterns, depending on the subtype (e.g., behavioral variant FTD often shows bilateral frontal lobe involvement, while semantic variant primary progressive aphasia shows left temporal lobe involvement).

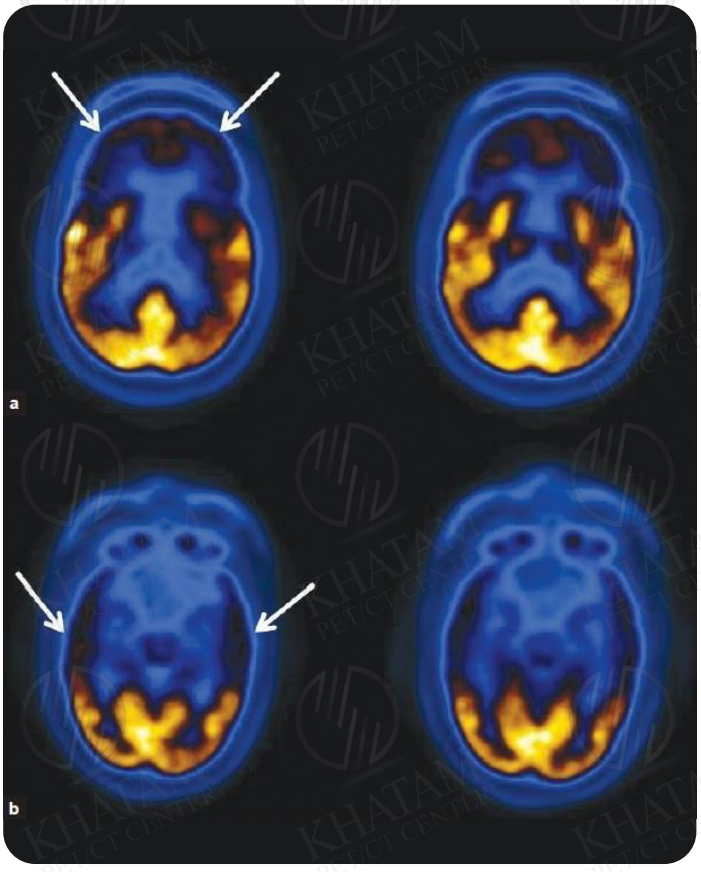

Figure 3. ^{18}F-FDG PET images in a 55-year-old female with FTD. Arrows indicate bilateral hypometabolism of the frontal (a) and temporal (b) cortex.

2- Amyloid and Tau PET:
Amyloid-PET (e.g., using tracers like florbetapir or florbetaben) is usually negative in FTD, similar to healthy controls, while tau-PET (e.g., using tracers like flortaucipir) may show uptake in some FTD subtypes, particularly those associated with tau pathology (e.g., progressive supranuclear palsy or corticobasal degeneration).

Dementia with lewy bodies (DLB)

DLB is a progressive neurodegenerative disorder characterized by the presence of Lewy bodies (abnormal protein deposits) in the brain.
PET/CT scans are not commonly used to diagnose DLB directly, but they can be part of a broader diagnostic approach. PET scans to predict risk or monitor disease progression are an area of ongoing research.

Diagnostic Use of PET/CT

1- ^{18}F-FDG PET/CT: :
It shows reduced glucose metabolism in the occipital cortex (a hallmark of DLB), unlike AD, which typically shows temporoparietal hypometabolism.

2- Dopamine Transporter (DaT) Tracers:
DaT scans (e.g., using ^{123}I-FP-CIT or ^{18}5F-DOPA) reveal reduced dopamine transporter activity in the striatum, supporting a diagnosis of DLB.

Brain Tumors

PET/CT imaging has become increasingly significant in neuro-oncology, providing critical insights into brain tumors that complement traditional imaging modalities like MRI. This imaging technique is particularly valuable for diagnosing, monitoring, and managing various types of brain tumors, including gliomas, meningiomas, primary central nervous system lymphomas (PCNSL), and brain metastases.

Clinical Applications of PET Imaging in Brain Tumors:

- Differential Diagnosis:
PET imaging aids in distinguishing between different types of brain tumors and non-neoplastic conditions. For example,^{18}F-FDG PET effectively differentiates PCNSL from glioblastomas due to the high uptake of FDG in lymphomas.

- Tumor Grading and Characterization:
Various radiotracers, such as amino acid tracers (e.g., ^{18}F-FET and ^{18}F-FDOPA), are utilized to assess tumor biology, helping to grade tumors and determine their metabolic activity non-invasively. For example,^{18}F-FDG PET effectively differentiates PCNSL from glioblastomas due to the high uptake of FDG in lymphomas.

- Monitoring Treatment Response:
PET is instrumental in evaluating how well a tumor responds to treatment. For instance, interim PET scans can predict treatment outcomes by assessing metabolic changes during therapy.

- Distinguishing Recurrence from Treatment Effects:
PET imaging can differentiate between true tumor progression and treatment-related changes, such as pseudoprogression or radiation necrosis, which is vital for appropriate patient management.

Radiotracers Used in Brain Tumor Imaging:

– ^{18}F-FDG:

- Measures glucose metabolism, which is often elevated in high-grade tumors.
- Limited in brain imaging due to high baseline glucose uptake in normal brain tissue and unspecific uptake in inflammatory, benign lesions.

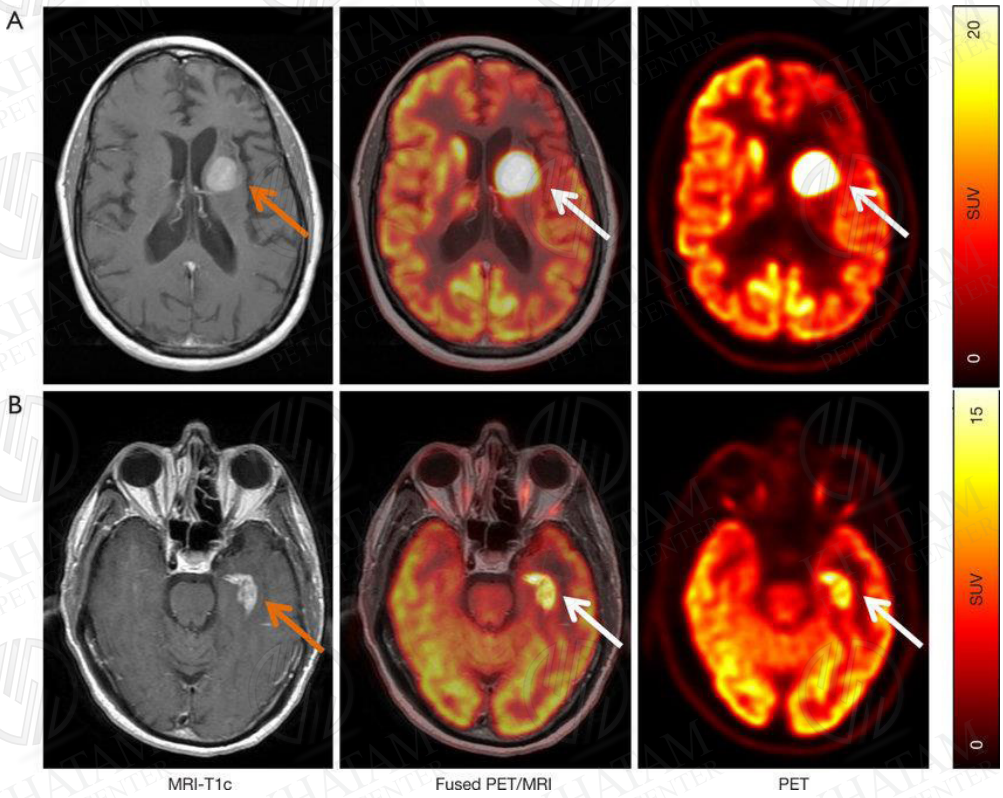

Figure 4. Representative cases of primary CNS lymphoma on FDG PET and MRI. (A) Contrast-enhanced T1-weighted MRI shows an enhancing lesion (left, orange arrow) in left corona radiata and superior basal ganglia, which demonstrate focal ^{18}F-FDG uptake on axial fused PET/MRI (middle, white arrows) and PET images. (B) Contrast-enhanced T1-weighted MRI depicts an enhancing lesion (left, orange arrow) at the left temporal horn; fused PET/MRI (middle, white arrow) and PET images confirmed focal ^{18}F-FDG uptake.

- Amino Acid Tracers (e.g., ^{18}F-FET, 11C-methionine):

- Better suited for brain tumors due to lower background uptake in normal brain tissue.
- Useful for visualizing tumor boundaries and assessing tumor activity.
- Radiolabeled amino-acid analogs were used for the imaging of glioma.

^{18}F-Fluoro-ethyl-l-tyrosine (FET) is transported through L-amino acid transporters (LAT), which are present in normal brain parenchyma. Their expression proportionately increases with the grade of glial proliferation. Thus, it has been considered the standard of care for differentiating between high-grade and low-grade glial tumors.

FET PET Imaging Indications:

- Guiding brain biopsy
- Diagnosis of primary brain tumors
- Directing radiotherapy
- Distinguishing between tumor recurrence and radionecrosis after initial therapy
- Evaluating response to therapy and for the prediction of patient outcome
- Delineate tumoral volume before radiotherapy
- To monitor the effects of radiotherapy and chemotherapy

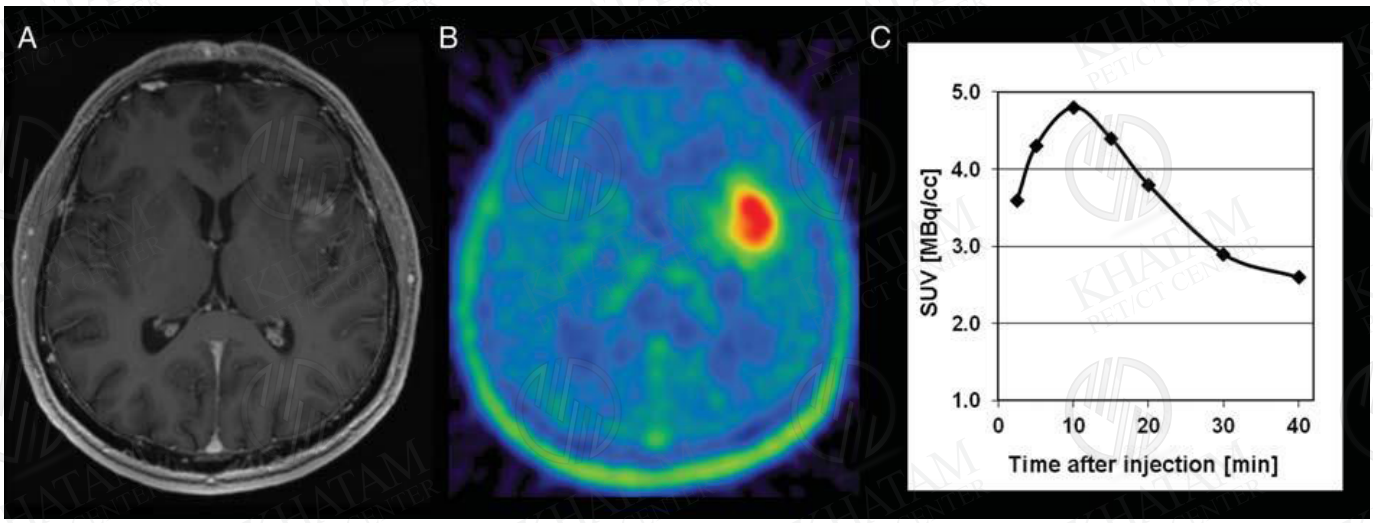

Figure 4. FET-PET analysis of an MRI-suspected anaplastic glioma. (A) Axial T1-weighted, contrast-enhanced MRI showing a contrast-enhancing, cortical, and subcortical left-sided insular lesion. (B) The co-registered axial FET-PET image reveals an intense tracer uptake with an SUVmax/BG of 5.0. (C) Dynamic analysis of FET-uptake within the. Histopathological and molecular-genetic evaluation revealed a WHO grade III astrocytoma.

^{68}Ga-DOTATATE:

- Used for meningiomas and other tumors expressing somatostatin receptors.

^{68}Ga-FAPI:

- FAPI targets the fibroblast activation protein (FAP), which is overexpressed in the tumor microenvironment of many cancers, including high-grade brain tumors, but is minimally present in normal brain tissue.
- FAPI uptake is prominent in high-grade gliomas (WHO grade III and IV), with little to no uptake in low-grade gliomas. This allows for noninvasive distinction between low- and high-grade tumors.
- FAPI PET can help differentiate true tumor recurrence from post-treatment changes, a common diagnostic challenge with MRI.
- FAPI PET has shown promise in detecting brain metastases and leptomeningeal involvement, sometimes revealing occult lesions not seen with other modalities.
- The high contrast of FAPI PET may assist in guiding biopsies and assessing surgical margins.
- FAP is being explored as a therapeutic target. Early studies have paired diagnostic FAPI PET with therapeutic radioligands, showing potential for targeted therapy in brain tumors.

Table: FAPI PET vs. Other Imaging in Brain Tumors

Feature	FAPI PET	Amino Acid PET (e.g., FET)	FDG PET
Uptake in Normal Brain	Minimal	Low	Moderate
Uptake in High-Grade Glioma	High	High	Variable
Uptake in Low-Grade Glioma	Low/None	Moderate	Low
Tumor-to-Background Ratio	Very High	High	Low
Utility in Recurrence	Promising	Established	Limited
Role in Therapy Planning	Emerging	Established	Limited
Theranostic Potential	Yes (experimental)	No	No

Epilepsy

PET/CT is an advanced imaging technique that plays a crucial role in the diagnosis and management of epilepsy, particularly in localizing epileptogenic foci. This method is particularly beneficial for patients with refractory epilepsy, where traditional imaging techniques like MRI may not provide conclusive results. ^{18}F-FDG PET/CT helps visualize glucose metabolism in the brain, allowing for effective localization of seizure foci.

Clinical Applications:

- Localization of Epileptogenic Focus:

PET scans measure metabolic activity in the brain using a radioactive tracer, typically FDG. In epilepsy, the epileptogenic focus (the area of the brain where seizures originate) often shows hypometabolism (reduced glucose uptake) during the interictal period (between seizures), helping to localize the seizure focus in drug-resistant epilepsy.

- Pre-Surgical Evaluation:

PET/CT is beneficial in patients with drug-resistant epilepsy who are being evaluated for surgical intervention. It helps identify the exact location of the epileptogenic zone, especially when MRI findings are inconclusive or normal. It can also help differentiate between lesional and non-lesional epilepsy, guiding surgical planning.

- Complementary to Other Modalities:

PET/CT is often used alongside other diagnostic tools, such as MRI, EEG, and SPECT, to provide a comprehensive picture of the epileptogenic zone. While MRI provides structural details, PET/CT adds functional information, improving diagnostic accuracy.

- Pediatric Epilepsy:

In children, where extratemporal epilepsy is more prevalent and often presents with normal MRI findings, PET/CT proves particularly useful. It can detect subtle metabolic changes related to conditions like cortical dysplasia, which is common in pediatric patients.

- Dual Pathology:

PET/CT can also assist in identifying dual pathology cases—where multiple seizure foci exist—by highlighting areas of hypometabolism that may indicate additional epileptic activity beyond the primary lesion.

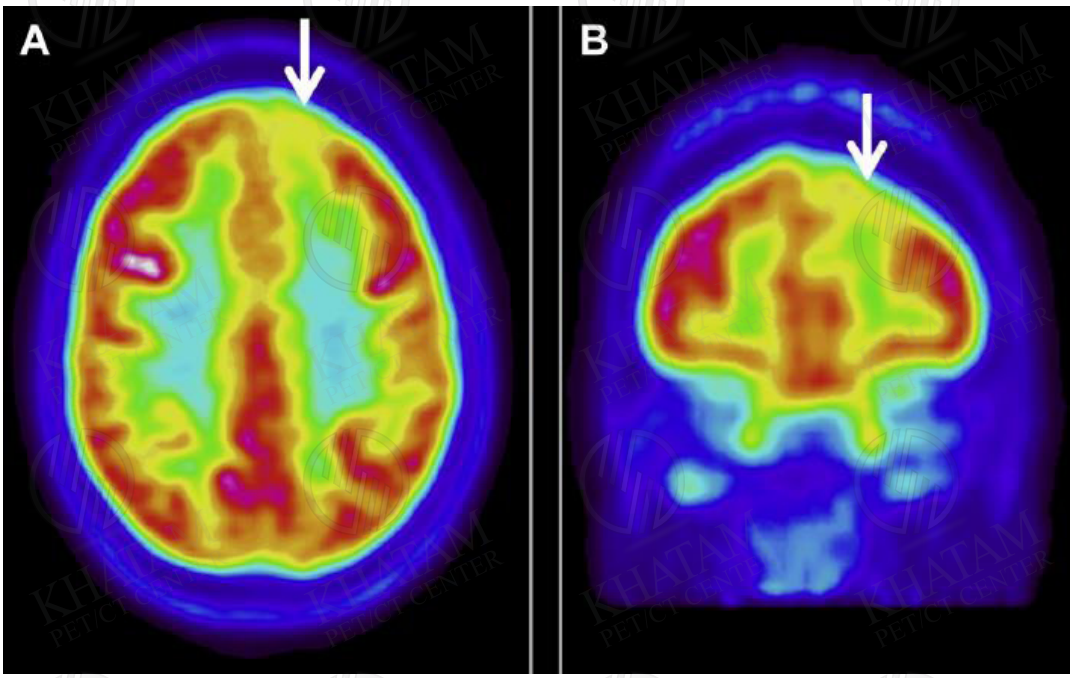

Figure 5. ^{18}F FDG PET of a 16-year-old girl with a history of frontal epilepsy refractory to antiepileptic drugs. The recent MRI was unremarkable. Video EEG showed frontal lobe seizures. A hypometabolic cortical region is visible in the left frontal cortex (white arrow) in axial (A) and coronal (B) images. This area was found to be related to the epileptogenic region.

Cerebrovascular Diseases:

PET/CT plays a significant role in assessing blood flow and metabolic activity in the brain, which is critical for understanding conditions like strokes and other circulatory disorders. By mapping these changes, clinicians can make informed decisions regarding treatment strategies.
PET/CT imaging holds significant promise for enhancing our understanding and management of cerebrovascular diseases. It can detect early pathological changes, assess brain function, and monitor treatment responses.

Common Tracers Used in PET/CT for Cerebrovascular Disease:

- ^{18}F-FDG:

Measures glucose metabolism, helpful in assessing brain activity and identifying areas of hypometabolism.

- ^{18}F-NaF (Sodium Fluoride):

Detects active calcification and inflammation in atherosclerotic plaques.

Key Applications of PET/CT:

- Detection of Atherosclerosis:

PET imaging, particularly with tracers like ^{18}F-NaF and ^{18}F-FDG, is pivotal in identifying atherosclerotic changes in carotid arteries. NaF-PET/CT has shown superior sensitivity in detecting early micro-calcifications associated with plaque formation, possibly contributing to cerebrovascular events. FDG-PET/CT complements this by assessing brain metabolic activity, providing insights into how these vascular changes affect cerebral function.

- Evaluation of Brain Metabolism:

PET imaging can quantify regional brain metabolism, helping to distinguish between different types of dementia, including vascular dementia. It allows for assessing metabolic disturbances that result from ischemic events and can identify areas of the brain that are at risk but not yet irreversibly damaged. This capability is crucial for planning interventions and predicting patient outcomes.

- Understanding Neuroinflammation:

PET scans can visualize neuroinflammation associated with cerebrovascular diseases, which plays a significant role in the progression of cognitive impairment. PET can detect inflammatory processes that may exacerbate conditions like stroke or contribute to vascular cognitive disorders using specific radioligands.

- Monitoring Therapeutic Interventions:

PET imaging helps monitor the effectiveness of therapeutic strategies in cerebrovascular disease. It can help evaluate changes in cerebral blood flow and metabolism following interventions such as surgical revascularization or medical management.

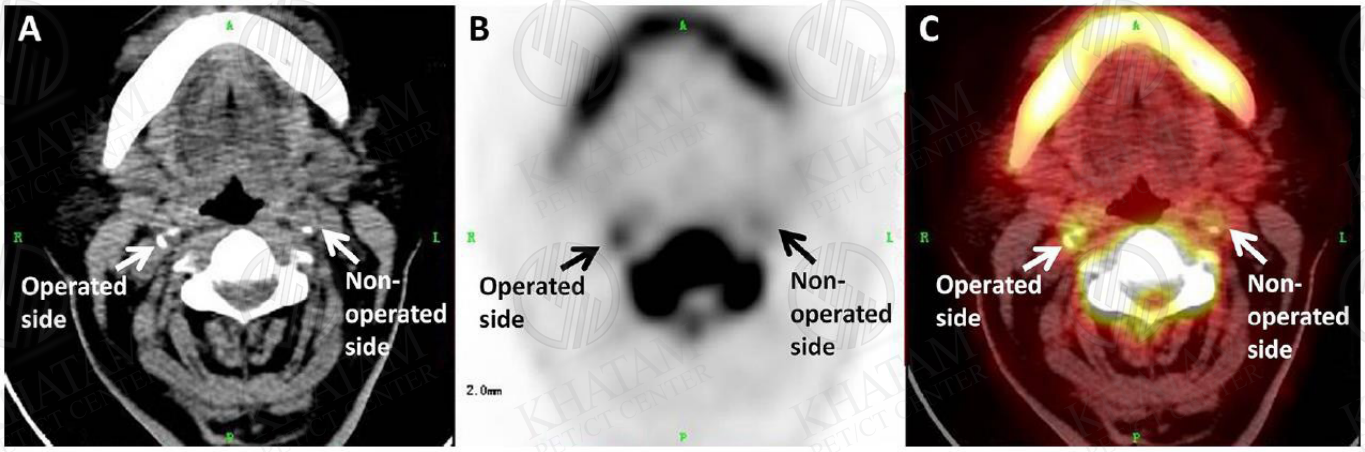

Figure 6. Transaxial ^{18}F-NaF PET-CT imaging of a patient whose right carotid artery was the operated side: (A) CT; (B) PET; (C) merged PET-CT images. CTA of the cerebral vessels confirmed that the stenosis rate of the right carotid artery was 90% and that of the left carotid artery was 30%. ^{18}F-NaF accumulated in the bilateral carotid artery plaques.

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^{18}F- Florbetapir PET/CT (Amyloid Imaging)

NEW ALZHEIMER TRACER

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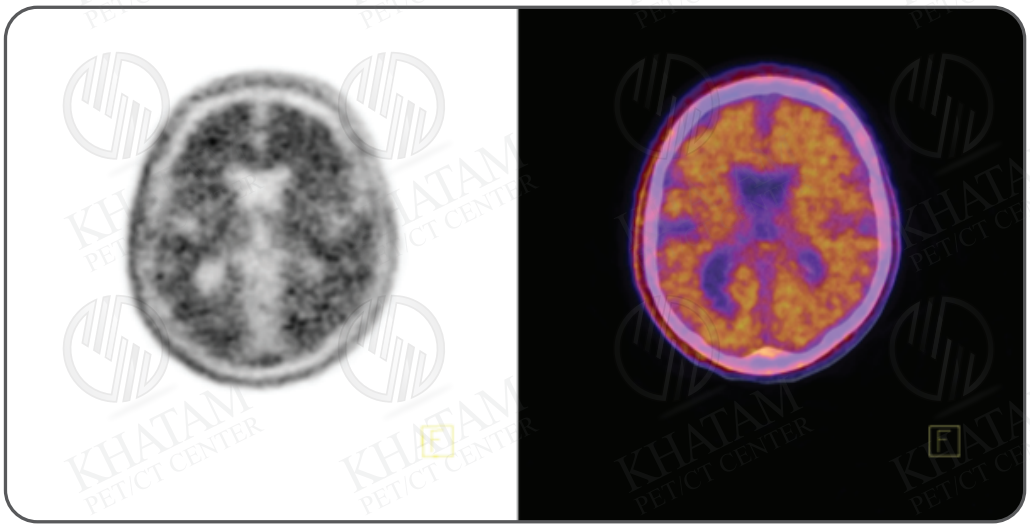
مرکز پت سی تی خاتم



Accurate Diagnosis & Tailored Alzheimer's Therapy

When To Consider Amyloid PET Imaging?

- Clinical uncertainty in patients with mild cognitive impairment
- Atypical presentations or suspected mixed dementia syndromes
- Early-onset progressive cognitive decline (65 years old or younger)
- Subjective Cognitive Decline (SCD), meeting SCD-plus criteria
- Determining eligibility for Lecanemab anti-amyloid therapy (FDA approved 2023)

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