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Positron Emission Tomography Imaging: An Updated Review for Radiologists.

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Abstract:

Background: Positron Emission Tomography (PET) is a cornerstone of functional and molecular imaging, enabling the visualization of metabolic and physiological processes in vivo. It utilizes radiotracers that accumulate in tissues with high biochemical activity, providing critical information beyond anatomical imaging. **Aim:** This updated review aims to synthesize the current applications, technological principles, and clinical significance of PET imaging for radiologists, highlighting its utility across various medical specialties and the emergence of novel radiotracers. **Methods:** The review consolidates evidence on PET procedures, including radiotracer administration, imaging protocols, and the integration with CT (PET-CT). It evaluates the use of different radiotracers—most notably 18F-FDG for glucose metabolism, 68Ga-DOTA peptides for neuroendocrine tumors, and specialized tracers for neurology and cardiology—across a broad spectrum of diseases. **Results:** PET imaging demonstrates high diagnostic and prognostic value. In oncology, it is indispensable for tumor staging, treatment response assessment, and detecting recurrence. In neurology, it aids in differentiating dementias and localizing epileptic foci. In cardiology, it accurately assesses myocardial viability. Emerging tracers, such as FAPI for cancer-associated fibroblasts, are expanding their diagnostic and theragnostic potential. Key considerations include managing interfering factors like patient diet and medication to ensure image accuracy.

Conclusion: PET imaging is a powerful, versatile modality that has revolutionized diagnostic medicine. Its ability to provide quantitative molecular data makes it essential for precision medicine, guiding diagnosis, treatment planning, and therapeutic monitoring across numerous clinical domains.

Keywords: Positron Emission Tomography (PET), Radiotracer, 18F-FDG, Molecular Imaging, PET-CT.

Introduction:

Positron emission tomography (PET) represents a sophisticated nuclear imaging modality extensively utilized in oncology for the assessment of metabolic and physiological functions within the human body. This technique relies on the administration of radiotracers, which facilitate the quantification and visualization of diverse metabolic activities, regional blood flow, and biochemical compositions in tissues, thereby allowing comprehensive evaluation of both normal and pathological processes [1]. Radiotracers can be delivered through various routes, including intravenous injection, oral ingestion, or inhalation, contingent upon the anatomical region under investigation and the metabolic characteristics of the targeted tissue. Once administered, these tracers distribute in the body according to tissue-specific affinities, permitting

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precise mapping of areas demonstrating heightened metabolic demand [2]. Tissues exhibiting increased metabolic activity demonstrate greater radiotracer accumulation, manifesting as hyperintense regions on PET images. The radiotracers employed in PET scanning contain unstable nuclei that undergo positron emission. These emitted positrons subsequently encounter electrons within adjacent tissues, resulting in annihilation events that produce pairs of gamma photons. These gamma rays are subsequently captured by an array of detectors arranged circumferentially around the patient within the PET scanner. Advanced computational algorithms reconstruct the collected signals into high-resolution three-dimensional images, providing a detailed spatial representation of tracer distribution across the body [3].

The selection of specific radiotracers is dictated by the biological process or cellular receptor of interest, enabling tailored imaging of processes such as glucose metabolism, amino acid transport, hypoxia, or receptor expression. PET imaging thus offers a unique combination of functional and molecular insight that extends beyond conventional anatomical imaging, allowing clinicians to detect early disease changes, evaluate tumor aggressiveness, monitor therapeutic response, and guide precision treatment planning. The integration of PET with other imaging modalities, such as computed tomography (CT) or magnetic resonance imaging (MRI), further enhances its diagnostic accuracy by correlating metabolic information with anatomical structures [1]. Through its capacity to provide quantitative and qualitative assessment of cellular activity, PET scanning has become an indispensable tool in contemporary oncologic imaging and research.

Procedures

The administration of the radiotracer in PET imaging can occur through multiple routes, including intravenous injection, oral ingestion, or inhalation, depending on the target organ or tissue and the specific diagnostic requirements. After administration, the tracer requires a variable uptake period to distribute throughout the body and localize within tissues according to their metabolic activity and receptor affinity. When a combined PET-computed tomography (PET-CT) examination is indicated, an additional contrast agent may be delivered either intravenously or orally to enhance anatomical delineation, providing complementary structural information alongside functional imaging. Patient positioning is determined by the anatomical region under investigation and is critical to ensuring accurate and reproducible imaging results. The PET scanner features a central bore through which the patient is guided into the imaging field, with care taken to maintain comfort and minimize motion, as even slight movements can degrade image quality [4].

Before full image acquisition, preliminary scout images are obtained to confirm the correct alignment and positioning of the patient within the scanner. Depending on the location of the target area and the nature of the study, patients may be instructed to hold their breath at specific intervals to reduce motion artifacts, particularly when imaging thoracic or abdominal regions. The scanning process itself typically requires a duration ranging from approximately thirty minutes to one hour, contingent upon the number of body regions being evaluated, the tracer used, and the imaging protocol established by the radiology team. During this period, the PET scanner detects gamma photons emitted from positron annihilation events, and sophisticated computational reconstruction generates three-dimensional images representing the distribution and intensity of tracer uptake. Careful adherence to procedural steps ensures high-quality images that can accurately reflect metabolic and functional characteristics of the tissues under investigation [5].

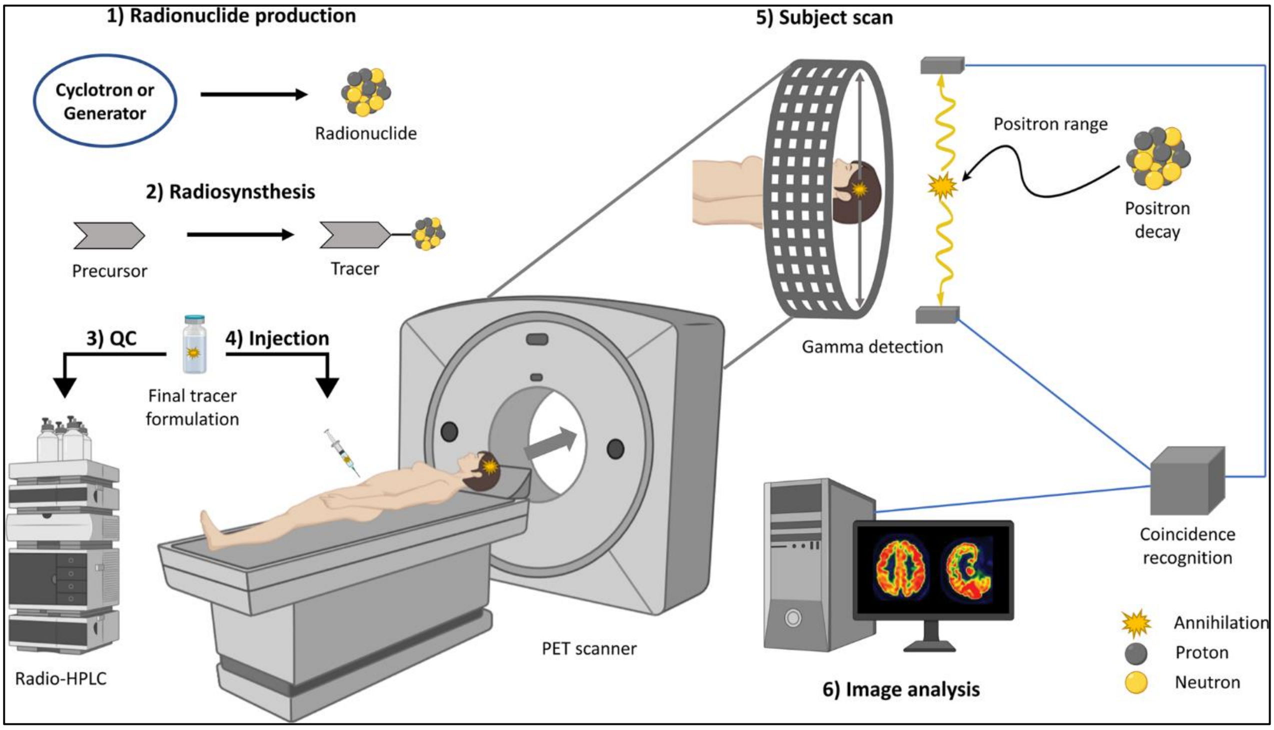

Figure 1: PET Preparation in Radiology.

Indications

Cancer:

Positron emission tomography (PET) scanning represents a highly specialized imaging modality that has established a central role in oncological diagnostics due to its capacity to provide precise functional and metabolic information about tissues. The most frequently utilized radiotracer in this domain is 18F-fluorodeoxyglucose (18F-FDG), a glucose analog that closely mimics physiological glucose and is actively transported into cells via glucose transporters. Upon entering the cell, 18F-FDG is phosphorylated by hexokinase enzymes, including the mitochondrial isoform, which is particularly elevated in rapidly proliferating cancer cells. This phosphorylation is a critical step that effectively traps the radiotracer within the cell because the absence of the hydroxyl group in 18F-FDG, replaced by radioactive fluorine, prevents its further metabolism through glycolysis. Consequently, tissues exhibiting elevated glucose utilization, such as malignant tumors, as well as metabolically active normal tissues, including the brain, liver, and kidneys, demonstrate pronounced radiotracer accumulation. This intracellular trapping, combined with the emission of positrons from 18F-FDG and subsequent annihilation events with electrons producing detectable gamma photons, allows for high-resolution three-dimensional imaging of metabolic activity, forming the basis for tumor detection, staging, and treatment monitoring. The radiation dose associated with 18F-FDG PET is approximately 7.5 mSv, while combined PET-computed tomography (PET-CT) examinations typically involve doses ranging from 14 to 30 mSv, depending on CT acquisition parameters [6].

In clinical oncology, FDG-PET is extensively employed for the diagnosis, staging, and therapeutic monitoring of a broad range of malignancies. Its use in hematologic cancers, particularly Hodgkin lymphoma [2,7] and non-Hodgkin lymphoma [3], has been well established, offering precise localization of disease sites, evaluation of metabolic activity, and assessment of therapeutic response. In pulmonary oncology, FDG-PET serves as an essential adjunct in the evaluation of solitary pulmonary nodules, providing diagnostic accuracy superior to conventional imaging [4,6]. Studies have reported a likelihood ratio for malignancy of 7.11 in cases of abnormal FDG uptake in solitary pulmonary nodules, underscoring its role in distinguishing malignant from benign lesions [7]. In non-small cell lung cancer (NSCLC), FDG-PET has demonstrated superior performance relative to CT in mediastinal staging. Specifically, PET achieves higher sensitivity (71% versus 43%), positive predictive value (44% versus 31%), negative predictive value (91% versus 84%), and overall accuracy (76% versus 68%) for the detection of N2 lymph node involvement. Although FDG-PET shows increased sensitivity (67% versus 41%) for N1 lymph nodes, its specificity (78% versus 88%) is slightly lower compared with CT. These diagnostic capabilities enable more accurate upstaging of patients with previously unrecognized metastases and downstaging of others, thereby refining treatment strategies, guiding surgical planning, and optimizing patient selection. However, FDG-PET is associated with limitations, including false-positive uptake in reactive or inflammatory lymph nodes and reduced detection capability for specific mediastinal stations, such as #5, #6, and #7. Nevertheless, FDG-PET is recommended for initial staging and evaluation of treatment response in FDG-avid lymphomas, encompassing subtypes such as diffuse large B-cell lymphoma, follicular lymphoma, and mantle cell lymphoma [8].

Beyond hematologic malignancies and lung cancer, FDG-PET has demonstrated significant utility in gastrointestinal oncology, though with certain limitations. In esophageal and gastroesophageal junction cancers, FDG-PET exhibits lower accuracy in detecting locoregional lymph node involvement (N1–N2) compared with the combined use of CT and endoscopic ultrasound (48% versus 69%), largely due to its reduced sensitivity (22% versus 83%) and limited spatial resolution for small periesophageal nodes [9]. Nonetheless, FDG-PET excels in detecting distant nodal and metastatic disease, facilitating accurate upstaging of 12% of patients from N1–N2 to M+Ly stage, although occasional false-negative downstaging may occur [10]. In colorectal cancer, FDG-PET has demonstrated high sensitivity in identifying primary tumors, particularly at a stage amenable to surgical resection. The technique can also detect premalignant colonic adenomas larger than 0.7 cm and provide metabolic characterization that may distinguish adenomas from carcinomas based on glycolytic activity. Despite these advantages, FDG-PET is not routinely employed as a primary screening tool for colorectal cancer due to the superior diagnostic and therapeutic capacity of colonoscopy, which allows for simultaneous lesion removal [11].

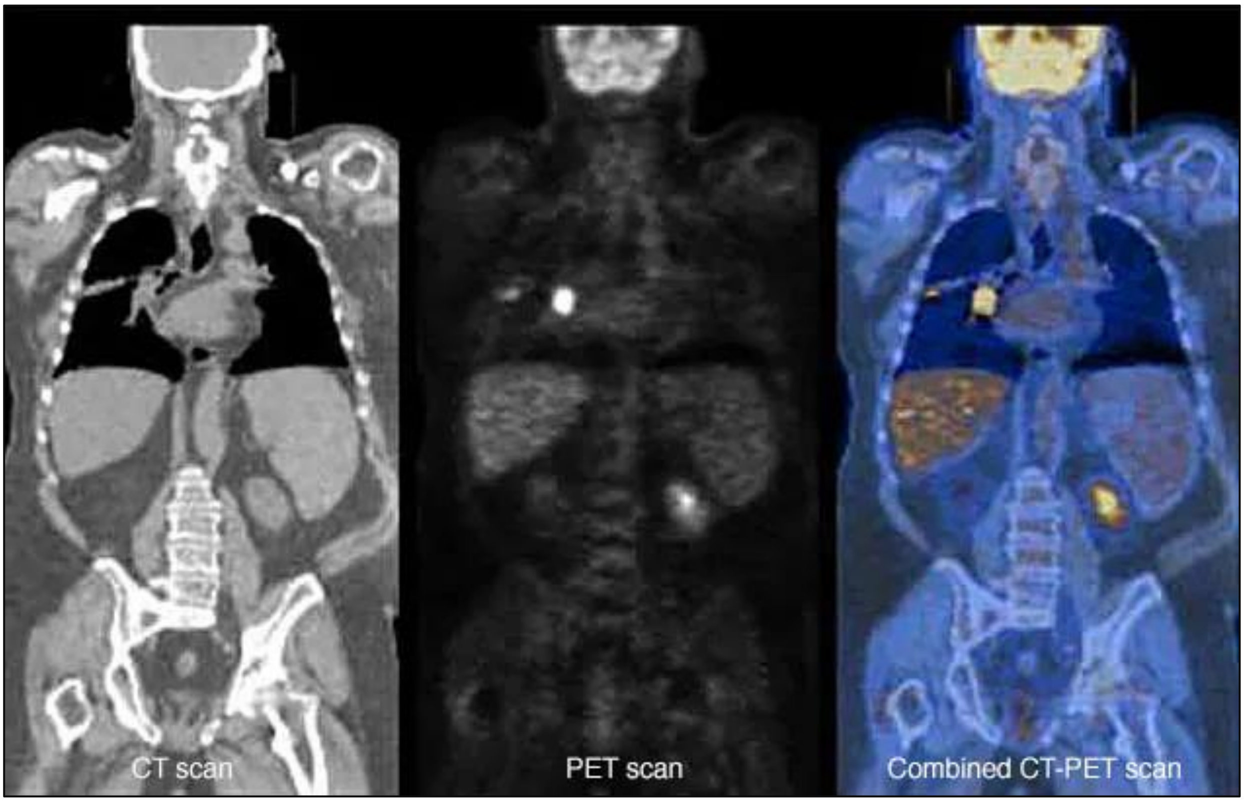

Figure 2: Comparison between CT, PET, and Combined CT-PET Scan.

FDG-PET has also proven indispensable in the detection of recurrent malignancy, particularly in cervical cancer. Whole-body PET scanning enables the identification of recurrent disease in both symptomatic and asymptomatic patients. Among asymptomatic women, recurrent cervical cancer was detected in 30% of cases, with PET demonstrating 80% sensitivity, 100% specificity, a positive predictive value of 100%, and a negative predictive value of 88.9%. In symptomatic women, detection rates were higher, with PET showing 100% sensitivity, 85.7% specificity, a positive predictive value of 93.3%, and a negative predictive value of 100% [12]. These findings illustrate the ability of FDG-PET to detect disease recurrence at an early stage, potentially before clinical symptoms manifest, thereby enabling timely therapeutic interventions and improving patient outcomes. The underlying mechanism of FDG accumulation in malignant tissues is attributed to the Warburg effect, which describes the preference of cancer cells for glycolysis over oxidative phosphorylation, even in the presence of sufficient oxygen. This metabolic reprogramming results in elevated glucose uptake and retention, which can be visualized by PET imaging. This principle not only allows tumor detection but also provides a quantitative measure of tumor activity, which is valuable for monitoring treatment response and assessing prognosis. FDG-PET's role in staging, restaging, and response assessment has led to its widespread incorporation into clinical protocols for various cancers, including lymphoma, lung cancer, esophageal carcinoma, colorectal malignancies, and cervical carcinoma [12].

In addition to its diagnostic and staging capabilities, FDG-PET is frequently utilized to guide tissue biopsy by identifying metabolically active regions within a tumor, ensuring representative sampling and improving diagnostic accuracy [9]. The modality's ability to integrate metabolic information with anatomical localization, particularly when combined with CT, enhances its utility in both pretreatment planning and post-treatment evaluation. FDG-PET provides clinicians with a dynamic and comprehensive view of tumor biology, surpassing the limitations of purely structural imaging modalities. Its use in detecting early metastatic spread, evaluating therapeutic efficacy, and assessing recurrence has fundamentally transformed oncologic imaging, making it an indispensable tool in contemporary cancer management[12]. In summary, FDG-PET scanning represents a cornerstone in oncological imaging, offering unparalleled insight into tumor metabolism, facilitating accurate staging, guiding biopsies, and monitoring treatment response. Its applications extend across a wide range of malignancies, including hematologic, thoracic, gastrointestinal, and gynecologic cancers. By capitalizing on the Warburg effect and the selective uptake of 18F-FDG, PET provides both qualitative and quantitative assessment of cancer activity, enabling precise therapeutic decision-making and improving clinical outcomes. Its integration into standard oncologic protocols has revolutionized patient management, supporting early detection of malignancy, evaluation of metastatic spread, and surveillance for recurrence. The combination of metabolic and anatomical imaging further enhances diagnostic precision, positioning FDG-PET as an essential modality in the modern oncologist's diagnostic armamentarium.

The gallium-68 (68Ga)-DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) peptide has emerged as a highly effective radiotracer for the detection of primary and metastatic neuroendocrine tumors (NETs). NETs are characterized by the expression of somatostatin receptors (SSTRs), with SSTR2 being the most abundantly expressed subtype, followed by SSTR1 and SSTR5. In contrast, SSTR4 and SSTR3 demonstrate lower levels of expression, approximately 36% and 23%, respectively [13,14]. The high affinity of 68Ga-DOTA peptides for these receptors underpins their diagnostic utility, particularly in cases where conventional anatomical imaging techniques fail to reveal the presence of lesions. Comparative studies have consistently demonstrated the superior sensitivity of 68Ga-DOTA PET-CT in detecting NET lesions. For instance, in patients with negative anatomical imaging, 68Ga-DOTA PET-CT identified significantly more lesions than 111In-octreotide imaging (30 versus 2; P = .028). Pfeifer et al reported a sensitivity of 88% for 111In-octreotide, which increased to 97% when utilizing copper-64 (64Cu)-DOTA PET-CT, highlighting the enhanced performance of these newer radiotracers [15]. Similarly, Srirajaskanthan et al found that 68Ga-DOTA PET-CT detected 74.3% of lesions compared to only 12% with 111In-octreotide [16], further reinforcing the superiority of 68Ga-labeled compounds for NET localization.

The clinical impact of 68Ga-DOTA PET-CT extends beyond simple lesion detection. This imaging modality has demonstrated remarkable efficacy in symptomatic patients with negative findings on anatomical imaging or endoscopic evaluation, regardless of biochemical evidence. In these contexts, 68Ga-DOTA PET-CT has significantly influenced clinical management, leading to alterations in therapeutic decisions and subsequent symptom improvement upon follow-up. Patients presenting with diagnostic uncertainty, particularly those with challenging or occult NETs, should be considered for 68Ga-DOTATATE PET-CT, as it offers highly sensitive localization and staging information [13]. Beyond 68Ga-DOTATATE, other radiotracers are also employed for targeted oncologic imaging. Carbon-11 (11C)-labeled metomidate (11C-metomidate) has demonstrated utility in detecting adrenocortical tumors, while 18F-DOPA PET-CT provides a more sensitive method for identifying and localizing pheochromocytomas compared to conventional meta-iodobenzyl guanidine (MIBG) scanning [17-20].

The development of novel tracers has expanded the potential applications of PET imaging in oncology. Quinoline-based tracers, particularly 68Ga-labeled fibroblast activation protein (FAP) inhibitors (FAPI), represent an emerging class of radiopharmaceuticals targeting cancer-associated fibroblasts predominantly found in tumor stroma. FAPI-PET improves lesion detection, particularly in organs such as the brain, liver, pancreas, and gastrointestinal tract, due to minimal background tracer retention in these regions. This low nonspecific uptake enhances lesion contrast and facilitates the identification of small metastatic or primary tumor sites. 68Ga-DOTA-FAPI PET has demonstrated higher sensitivity and specificity in colorectal cancer staging, allowing for more accurate assessment of primary tumors and metastatic spread [21]. Its application in lung cancer has similarly enhanced the precision of staging and metastatic evaluation, with improved detection of nodal, brain, bone, and pleural metastases. The integration of the DOTA chelator into the FAPI framework permits the conjugation of therapeutic radioisotopes such as yttrium-90, thereby enabling a theranostic approach that combines diagnostic imaging with targeted radionuclide therapy. This dual capability holds significant promise for personalized oncologic management, particularly in tumors with prominent stromal components [21,22].

In breast cancer, studies have explored the role of FAPI-PET in evaluating pathological response to therapy, highlighting its potential to guide treatment decisions and monitor therapeutic efficacy [23,24]. Moreover, the application of radiolabeled monoclonal antibodies, such as 89Zr-girentuximab, has emerged as a valuable tool for characterizing specific tumor subtypes, including the clear cell variant of renal cell carcinoma [25]. These advances illustrate the growing versatility of PET imaging in oncologic diagnostics, allowing for precise molecular characterization of tumors and improving the accuracy of staging and treatment planning.

68Ga-DOTA PET-CT not only facilitates the identification of lesions that are occult on anatomical imaging but also contributes to prognostic stratification. By quantifying receptor expression and metabolic activity, this modality provides critical information regarding tumor biology, aggressiveness, and potential response to therapy. This capability is particularly relevant in NETs, where somatostatin receptor density can guide the use of peptide receptor radionuclide therapy (PRRT), enabling targeted treatment based on receptor expression profiles. The combination of sensitive lesion detection and the ability to assess receptor status underscores the integral role of 68Ga-DOTA PET-CT in the modern management of NET patients [23-25].

The adoption of newer radiotracers, including FAPI and 89Zr-labeled agents, has broadened the scope of PET imaging, extending its utility beyond NETs to solid tumors with prominent stromal components or specific molecular targets. FAPI-PET, in particular, has demonstrated exceptional ability to detect lesions in organs where conventional tracers may be limited due to physiological uptake or low receptor expression. This modality's ability to identify small and otherwise elusive metastatic deposits enhances staging accuracy and informs clinical decision-making, including surgical planning, systemic therapy selection, and monitoring of treatment response. In addition, the integration of diagnostic and therapeutic capabilities through theranostic applications represents a significant advancement in personalized oncology, allowing clinicians to deliver targeted radionuclide therapy directly to tumor sites identified on PET imaging [24,25]. Overall, 68Ga-DOTA PET-CT and related novel radiotracers represent a major advancement in oncologic imaging, providing high sensitivity and specificity for lesion detection, enabling precise molecular characterization, and facilitating theranostic applications. In NETs, this imaging modality surpasses conventional anatomical imaging and traditional radiotracers such as 111In-octreotide, offering superior lesion localization and staging accuracy [13-16]. The incorporation of novel tracers such as FAPI and 89Zr-labeled antibodies further expands the diagnostic and therapeutic potential of PET imaging, improving outcomes across a range of malignancies, including colorectal, lung, breast, and renal cell cancers [21,22,24,25]. As PET technology continues to evolve, its integration into personalized oncology protocols will be increasingly important, guiding targeted interventions, optimizing therapeutic response, and supporting the development of individualized treatment strategies tailored to tumor biology and receptor expression [25].

This comprehensive evaluation highlights the pivotal role of 68Ga-DOTA PET-CT and emerging PET tracers in contemporary oncologic practice, demonstrating their ability to detect occult lesions, inform treatment planning, and support personalized therapeutic approaches. Through enhanced sensitivity, specificity, and theranostic capability, these modalities are reshaping the landscape of tumor imaging, providing clinicians with precise tools to improve patient outcomes, advance research, and implement evidence-based interventions tailored to individual tumor biology. The evolution of PET imaging underscores the transition from purely anatomical assessment to a fully integrated functional and molecular diagnostic approach, establishing PET as an indispensable modality in the management of both neuroendocrine and solid organ malignancies.

Neurology:

Positron emission tomography (PET) has become an indispensable tool in neurology due to its ability to provide in vivo functional and molecular imaging of the brain, allowing for precise characterization of neurological disorders at a biochemical and physiological level. Areas exhibiting high radiotracer uptake on PET scans correlate with elevated regional brain activity and can serve as indirect measures of cerebral blood flow. Oxygen-15 is commonly employed as a tracer for evaluating regional perfusion, reflecting areas of heightened neuronal activity. In neurodegenerative disorders such as Alzheimer's disease, PET imaging reveals a marked reduction in glucose and oxygen metabolism across affected regions, reflecting synaptic dysfunction and neuronal loss. 18F-fluorodeoxyglucose (18F-FDG) PET is extensively used in this context, offering a robust method for differentiating Alzheimer's disease from other dementias based on patterns of hypometabolism. The assessment of perfusion, glucose metabolism, and amyloid-beta deposition has been integrated into the revised diagnostic criteria for Alzheimer's disease as essential biomarkers. Specific amyloid-targeting tracers, including florbetapir F18, flutemetamol F18, and florbetaben F18, facilitate the detection and quantification of amyloid-beta plaques, providing both diagnostic and prognostic information. Additional PET targets under investigation include tau protein accumulation and markers of neuroinflammation, which contribute to disease progression and clinical symptomatology [26].

At a molecular level, protein kinase C (PKC) is involved in the non-amyloidogenic processing of amyloid precursor protein (APP) by promoting the induction of alpha-secretase, also referred to as "a disintegrin and metalloprotease (ADAM)." This pathway prevents the formation of neurotoxic amyloid-beta fragments and is crucial for memory acquisition and maintenance. PKC deficits are observed early in Alzheimer's disease, preceding overt clinical symptoms. Recent developments have enabled the radiolabeling of selective PKC inhibitors, such as Enzastaurin (LY317615), with carbon-11 (11C), providing a potential PET probe for evaluating PKC activity in vivo [26]. P-glycoprotein (P-gp) at the blood-brain barrier (BBB) is implicated in amyloid-beta clearance, and PET imaging using [11C] verapamil, a P-gp substrate, has demonstrated age-dependent variations in transporter expression, with lower levels observed in individuals aged 75 and older and higher levels in younger populations [26]. These studies highlight the capacity of PET to provide insights into mechanisms underlying protein misfolding, impaired clearance, and synaptic dysfunction [27].

PET imaging also allows for the evaluation of cholinergic deficits in neurodegenerative diseases. Radiolabeled acetylcholine analogs, such as N-[(11)C]-methyl-4-piperidyl acetate (MP4A), reveal reductions in cortical acetylcholine activity in Alzheimer's disease, with more pronounced decreases in the posterior cingulate gyrus in patients with Lewy body dementia [28]. Radiolabeled cholinesterase inhibitors, including [11C]donepezil, permit the visualization of therapeutic binding sites, facilitating the assessment of drug-target interactions in vivo. Fluorinated tracers, such as 3-(benzyloxy)-1-(5-[18F]fluoropentyl)-5-nitro-1H-indazole ([18F]-IND1), structurally related to the acetylcholinesterase inhibitor CP126,998, have been developed to detect alterations in acetylcholinesterase activity in Alzheimer's disease [29,30]. These approaches enhance our understanding of synaptic deficits, guide therapeutic interventions, and allow for longitudinal monitoring of disease progression [29,30].

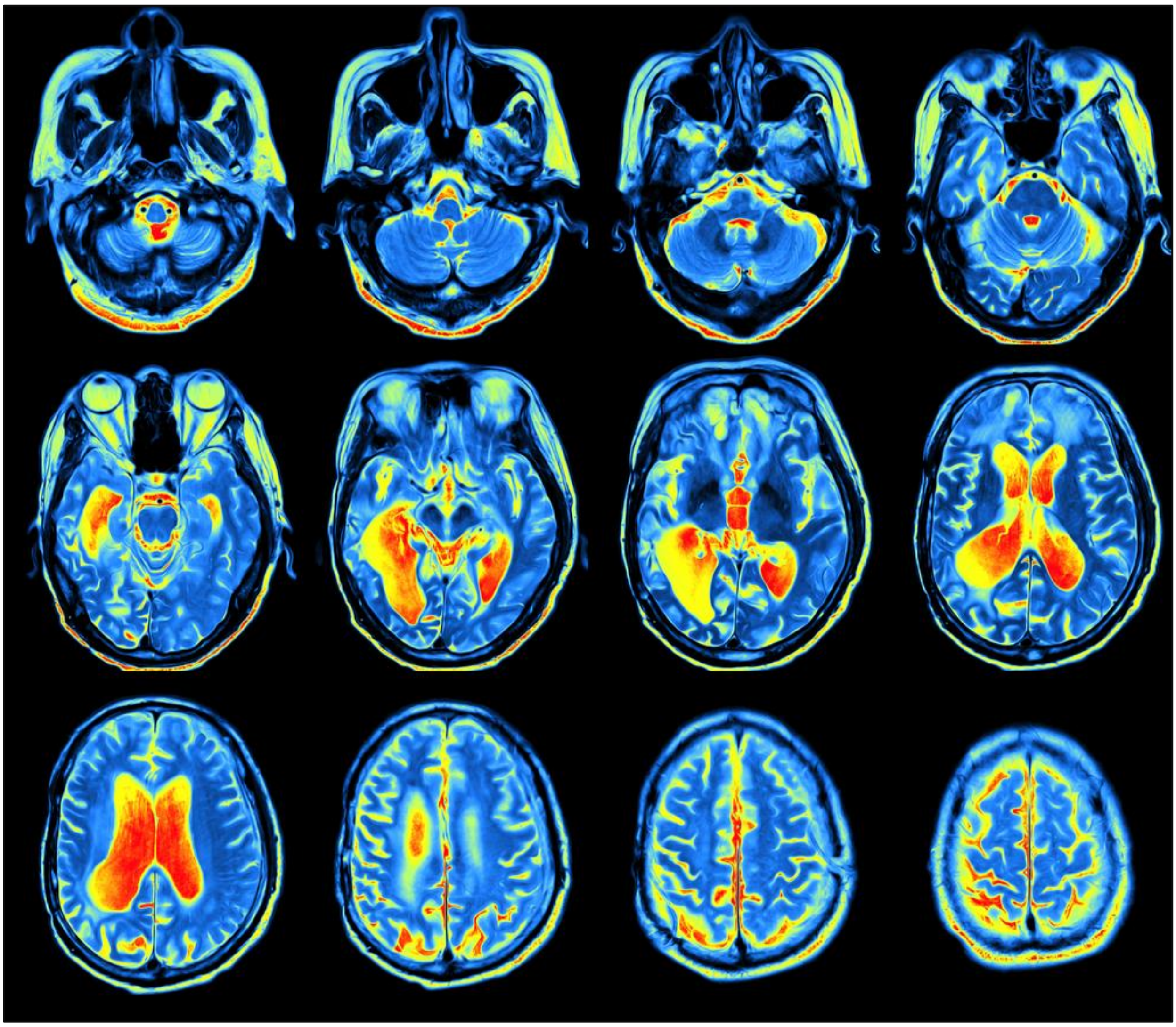

Figure 3: PET Scanning in Neurology.

Beyond Alzheimer's disease, PET has proven invaluable in the study and differential diagnosis of atypical Parkinsonism disorders. FDG-PET enables the visualization of regional metabolic changes characteristic of these conditions, supporting their distinction from idiopathic Parkinson disease [31]. Similarly, PET is routinely employed in epilepsy evaluation for the localization of seizure foci, which typically exhibit hypometabolism during interictal periods. This capability allows for precise surgical planning and targeted interventions, particularly in refractory cases. PET tracers targeting specific neuroreceptors have further expanded their utility in neurological research and clinical practice. Radioligands such as 11C-raclopride, 18F-fallypride, and 18F-desmethoxyfallypride allow mapping of dopamine D2/D3 receptor distribution and function. Serotonin transporter imaging can be performed using 11C-McN 5652 and 11C-DASB, while 18F-mefway targets serotonin 5HT1A receptors. Nicotinic acetylcholine receptors can be visualized using 18F-nifene, and aromatic L-amino acid decarboxylase (AADC) activity can be mapped with 6-FDOPA. These radiotracers provide detailed information about neurotransmitter systems implicated in neurodegenerative, psychiatric, and movement disorders, enabling mechanistic studies and supporting clinical decision-making [31].

PET scanning has also contributed significantly to neuropsychology by linking cognitive processes to regional brain activity. Functional correlations between task-specific activation and tracer uptake allow for the identification of neural substrates underlying memory, attention, executive function, and other higher-order cognitive processes. In psychiatry, PET radiotracers targeting dopamine, serotonin, opioid, and cholinergic receptors have elucidated neurochemical alterations associated with depression, schizophrenia, anxiety disorders, and substance use disorders. This information supports the development of novel pharmacologic interventions and enables monitoring of treatment efficacy at a molecular level [31].

In the domain of neurosurgery, PET has been integrated into stereotactic and radiosurgical procedures. PET-guided imaging allows for precise localization of targets in functional neurosurgery, tumor resection, and radiosurgical ablation. By combining metabolic information with structural imaging modalities such as MRI and CT, PET provides a comprehensive map of disease involvement, guiding accurate lesion targeting while minimizing injury to surrounding healthy tissue. This is particularly valuable in epilepsy surgery, movement disorder interventions, and the management of brain tumors, where PET improves both surgical outcomes and postoperative functional preservation [29-31].

Overall, PET imaging has transformed the understanding and management of neurological disorders by providing quantitative, spatially resolved information about brain metabolism, neurotransmitter systems, receptor expression, and protein deposition. In Alzheimer's disease, it enables early diagnosis, differentiation from other dementias, and evaluation of therapeutic responses through amyloid, tau, perfusion, and cholinergic imaging. In movement disorders, PET supports differential diagnosis, elucidates pathophysiological mechanisms, and informs clinical decision-making. In epilepsy, it localizes seizure foci for surgical planning, while in psychiatry, it allows for characterization of neurotransmitter abnormalities underlying diverse psychological conditions. Additionally, PET facilitates the integration of neuroimaging into surgical planning, radiosurgery, and targeted interventions, improving outcomes while reducing risk to healthy tissue [26-31]. The continuous development of novel radiotracers targeting specific molecular pathways—including amyloid-beta, tau, acetylcholinesterase, PKC, P-gp, and various neurotransmitter receptors—enhances the diagnostic, prognostic, and therapeutic potential of PET in neurology. These advances support personalized medicine by linking molecular pathology to clinical presentation, guiding treatment selection, and monitoring therapeutic efficacy. PET's ability to combine functional, molecular, and structural information establishes it as an indispensable modality for research and clinical practice in neurology, neuropsychology, psychiatry, and neurosurgery. Its integration into multi-modal imaging protocols ensures precise localization, mechanistic understanding, and improved patient outcomes, while continuing innovations in tracer development promise further expansion of its clinical and research applications [26-31].

Cardiology

Positron emission tomography (PET) has become a pivotal modality in cardiology, providing insights into myocardial metabolism, perfusion, and inflammation, which are essential for the diagnosis, risk stratification, and management of various cardiac conditions. One of the primary applications of PET in cardiology involves the identification of hibernating myocardium using [18F]fluorodeoxyglucose ([18F]FDG). Hibernating myocardium represents areas of chronically ischemic yet viable cardiac tissue that exhibit reduced contractile function but retain the potential for recovery following revascularization. [18F]FDG-PET identifies these regions by demonstrating increased glucose uptake, reflecting a metabolic shift toward anaerobic glycolysis in response to ischemia. This metabolic assessment is crucial in determining the potential benefits of coronary revascularization and in guiding therapeutic decision-making, particularly in patients with chronic ischemic heart disease. Additionally, [18F]FDG-PET has emerged as a valuable tool for imaging atherosclerosis, enabling the early detection of vascular inflammation in patients at risk of stroke. By visualizing metabolic activity within the vessel wall, PET allows for the identification of inflammatory changes before morphological alterations or irreversible vascular damage occurs, thus supporting early intervention strategies, including pharmacologic and lifestyle modifications. However, this technique is limited by the inherently high physiological uptake of [18F]FDG in the myocardium, which can reduce specificity and complicate interpretation [32,33].

PET imaging also plays a central role in the assessment of myocardial perfusion. Multiple radiotracers have been developed to measure myocardial blood flow, including 13N-labeled ammonia, oxygen-15–labeled water ([15O]-H2O), 82Rb-chloride, and 62Cu-labeled pyruvaldehyde bis(N4-methylthio-semicarbazone) (62Cu-PTSM). Among these, 13N-ammonia and 82Rb are the only agents approved by the US Food and Drug Administration (FDA) for clinical use, and they provide reliable quantification of regional and global myocardial perfusion [34]. These tracers allow for the evaluation of perfusion deficits caused by coronary artery disease, the assessment of collateral circulation, and the identification of ischemic territories that may benefit from revascularization. PET-derived perfusion measurements also enable accurate quantification of myocardial blood flow and coronary flow reserve, which are predictive of adverse cardiovascular events and can inform individualized patient management strategies.

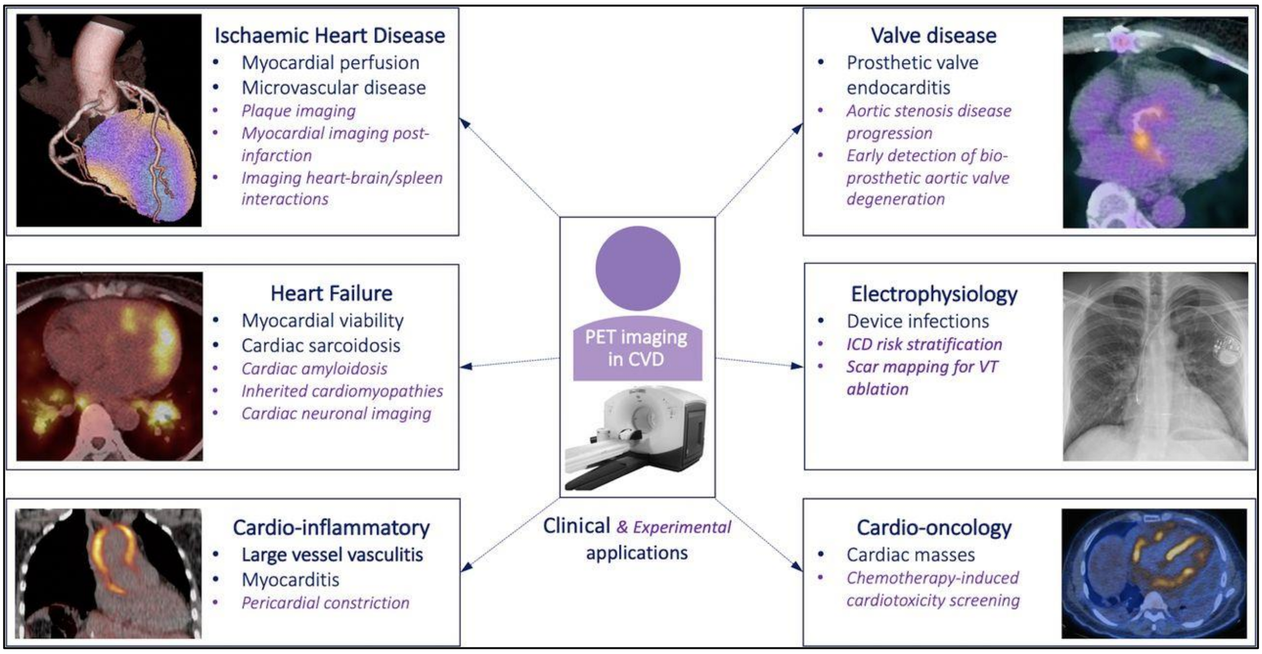

Figure 4: PET Scanning in Cardiology.

In addition to perfusion imaging, PET is instrumental in evaluating myocardial metabolism. Under normal conditions, the heart primarily relies on free fatty acids for oxidative metabolism. However, in ischemic or hypoxic conditions, myocardial tissue shifts toward glucose utilization due to increased anaerobic glycolysis. This metabolic adaptation can be visualized using tracers such as [18F]-FDG and 11C-labeled palmitate or acetate. Combining perfusion imaging with [18F]-FDG enables precise assessment of myocardial viability, which is regarded as the gold standard in viability evaluation. PET imaging can accurately predict functional recovery following revascularization, improvements in congestive heart failure symptoms, exercise tolerance, and overall quality of life. Furthermore, PET-derived viability data correlate with long-term clinical outcomes, including cardiac remodeling, recurrent cardiac events, and survival, providing comprehensive prognostic information that informs therapeutic planning [34]. The integration of perfusion and metabolic imaging with PET also allows for personalized treatment approaches. Patients with regions of reduced perfusion but preserved metabolic activity, indicating hibernating myocardium, may be prioritized for revascularization procedures. Conversely, areas exhibiting both perfusion and metabolic deficits are likely non-viable and may not benefit from interventional strategies. This dual assessment enhances clinical decision-making, minimizes unnecessary interventions, and optimizes patient outcomes. Moreover, PET imaging can be applied to monitor responses to pharmacologic therapies aimed at improving myocardial perfusion and function, offering an objective measure of therapeutic efficacy.

In summary, PET has transformed cardiology by providing detailed, non-invasive visualization of myocardial perfusion, metabolism, and inflammatory activity. The use of [18F]FDG for detecting hibernating myocardium and vascular inflammation, in combination with perfusion tracers such as 13N-ammonia and 82Rb, offers a comprehensive approach to diagnosing and managing ischemic heart disease, large-vessel vasculitis, and other cardiovascular disorders. PET's ability to quantify metabolic shifts and perfusion deficits supports informed clinical decision-making, predicts functional recovery, guides therapeutic interventions, and informs prognosis. Its role in assessing myocardial viability, exercise capacity, cardiac remodeling, and long-term survival underscores its status as the gold standard for evaluating myocardial viability and its growing importance in contemporary cardiovascular care [32-34].

Infectious Diseases

Positron emission tomography (PET) has become an increasingly valuable tool in the detection and characterization of infectious processes, largely due to its capacity to visualize metabolic and inflammatory changes associated with infection. The most commonly employed radiotracer in this context is [18F]fluorodeoxyglucose ([18F]FDG), which accumulates in regions of increased glucose metabolism, a hallmark of inflammatory cell activity. This property allows PET imaging to identify infection-associated inflammatory responses, even in cases where conventional imaging techniques fail to detect structural abnormalities. In addition to FDG, specific tracers have been developed to target bacterial pathogens directly, including [18F]maltose, [18F]maltohexaose, and 2-18F-fluorodeoxysorbitol (FDS), with FDS exhibiting selective uptake by Enterobacteriaceae [24,35]. These pathogen-specific tracers enable precise localization of bacterial infections, which is particularly useful in complex clinical scenarios where conventional imaging may be insufficient.

Clinical applications of PET in infectious diseases are broad. FDG-PET is particularly useful for evaluating fever of unknown origin (FUO), allowing for rapid localization of occult infections. In vascular graft infections, FDG-PET provides high-resolution images that facilitate both diagnosis and preoperative planning. In musculoskeletal infections such as osteomyelitis, joint prosthesis infections, and diabetic foot infections, FDG-PET demonstrates superior spatial resolution compared to single-photon emission-computed tomography (SPECT), enhancing lesion localization and characterization. Integration of PET with computed tomography (CT) further improves anatomical correlation, allowing clinicians to distinguish infection from post-surgical or post-traumatic changes [36]. FDG-labeled leukocyte imaging represents another PET-based technique, providing results comparable to 111In-oxine–labeled leukocyte scintigraphy in the detection of infections. This approach has been applied to vascular graft evaluation, colonic inflammation assessment, and the diagnosis of peritoneal tuberculosis, demonstrating PET's versatility in both acute and chronic infectious settings [37-41].

Autoimmune Diseases

In the evaluation of autoimmune diseases, PET imaging has emerged as an important tool for diagnosis, monitoring, and treatment planning. Immunoglobulin G4 (IgG4)-related disease, a systemic fibro-inflammatory condition, can be effectively assessed using FDG PET-CT, which identifies metabolically active lesions and guides biopsy. While PET is not currently standard in sarcoidosis evaluation, it has demonstrated utility for initial diagnosis, disease monitoring, and assessment of cardiac involvement, providing both functional and structural information that complements conventional imaging. PET can also guide biopsy site selection by identifying active granulomatous tissue, thereby improving diagnostic yield [42].

In autoimmune thyroid diseases, FDG-PET is able to differentiate normal thyroid parenchyma from diffuse inflammatory changes, facilitating early diagnosis and monitoring of disease progression [43]. Rheumatologic applications of PET include the assessment of disease activity in rheumatoid arthritis, where FDG uptake in affected joints correlates with clinical parameters such as pain, swelling, and laboratory markers of inflammation. This quantitative measure of metabolic activity can be used to monitor therapeutic response, offering an objective assessment tool for treatment efficacy. Furthermore, FDG-PET has demonstrated high diagnostic value in distinguishing polymyalgia rheumatica from rheumatoid arthritis, conditions that may present with overlapping clinical features [44]. PET imaging is also increasingly used to monitor large-vessel vasculitis, as reduced arterial FDG uptake has been observed in patients achieving clinical remission, providing an objective biomarker for therapeutic monitoring [45].

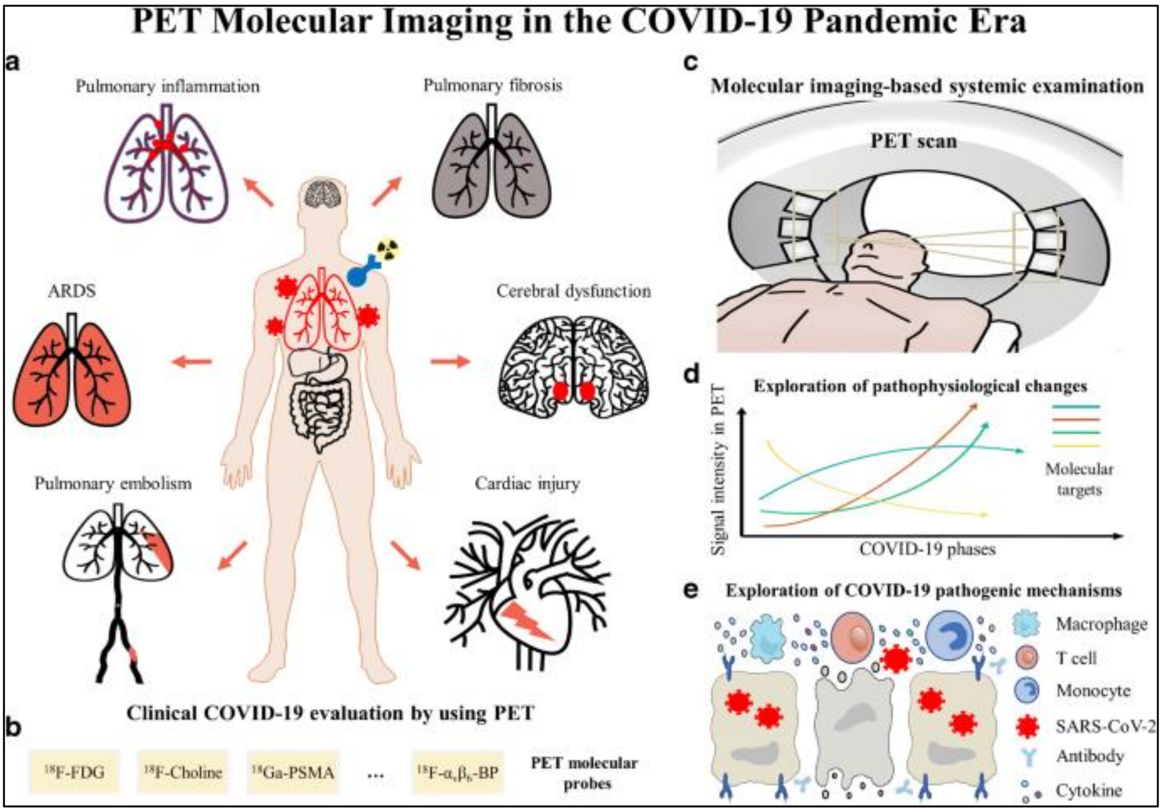

Figure 5: PET scanning for infectious diseases such as COVID-19.

Musculoskeletal System Diseases

PET imaging provides unique advantages in the evaluation of musculoskeletal disorders, particularly in assessing deep-lying muscles that are inaccessible to surface-based techniques such as electromyography. PET enables visualization of metabolic activity in these muscles during functional activation, providing insights into neuromuscular physiology and pathology. In addition, PET tracers targeting bone metabolism, such as [18F]-sodium fluoride ([18F]-NaF), have become instrumental in the evaluation of bone disorders. [18F]-NaF accumulates in areas of increased bone turnover, reflecting regional bone metabolism and perfusion. This capability has been leveraged to study bone metastases, offering superior detection and characterization compared to conventional bone scintigraphy [46]. PET-based assessment of musculoskeletal disease provides clinicians with quantitative data that can guide treatment planning, monitor response to therapy, and predict disease progression, enhancing patient management across a range of orthopedic and oncologic conditions.

Overall, PET imaging provides a highly sensitive and versatile tool for evaluating infectious, autoimmune, and musculoskeletal diseases. In infectious conditions, FDG-PET and pathogen-specific tracers allow early detection, precise localization, and differentiation from non-infectious inflammation. In autoimmune disorders, PET provides insight into disease activity, guides biopsy selection, and supports monitoring of treatment response, while in musculoskeletal conditions, PET enables functional assessment of deep muscle activity and detection of bone metabolic changes. The integration of PET with CT or other anatomical imaging modalities further enhances diagnostic accuracy, allowing for comprehensive evaluation of disease burden and facilitating personalized therapeutic strategies. Across these domains, PET imaging represents a significant advance in both diagnostic and clinical management, offering functional and molecular insights that complement structural imaging techniques, ultimately improving patient outcomes and supporting evidence-based decision-making [23,35-38].

Interfering Factors

Several factors can significantly affect the accuracy and reliability of PET imaging. Strenuous physical activity before the scan can increase radiotracer uptake in muscles and other tissues, potentially confounding image interpretation. To minimize these effects, patients are advised to avoid intense exercise before the procedure [47]. Dietary preparation is also critical. A low-carbohydrate, sugar-free diet is recommended for at least 24 hours before imaging. Permissible foods include protein-rich items such as meat, cheese, and eggs, as well as non-starchy vegetables. In contrast, foods high in carbohydrates, including cereals, pasta, bread, milk, and sugar-containing products, should be avoided, as they can alter glucose metabolism and interfere with tracer distribution. Additionally, patients should fast for a minimum of six hours before the scan to ensure consistent radiotracer uptake [47]. The presence of metal objects, including jewelry, piercings, or clothing with metallic components, can interfere with PET imaging and should be removed before scanning. Several physiological and pharmacological factors may also compromise scan accuracy. High blood glucose levels, particularly in diabetic patients, can reduce tracer uptake in target tissues and obscure pathology. Consumption of caffeine, alcohol, or tobacco within 24 hours of the scan can alter metabolic activity and tracer distribution. Psychological and neurological factors, such as anxiety or conditions that impair the ability to remain still, can negatively impact image quality, particularly in brain imaging. Certain medications, including insulin, tranquilizers, and sedatives, may modify metabolic activity or interfere with tracer uptake. Clinicians must consider these variables and provide clear pre-scan instructions to optimize PET imaging quality, ensuring that physiological, pharmacological, and behavioral factors do not compromise diagnostic accuracy [47,48].

Complications

Positron emission tomography-computed tomography (PET-CT) is generally considered a safe imaging modality, but several complications and safety considerations must be acknowledged. One of the primary risks associated with PET-CT arises from the administration of contrast agents used in the CT component of the scan. Intravenous contrast carries the potential for hypersensitivity reactions, ranging from mild allergic responses to severe anaphylaxis. Although rare, these reactions can be life-threatening and require immediate medical intervention. Another concern is contrast-induced nephropathy, particularly in patients with preexisting renal impairment, where contrast media may exacerbate kidney dysfunction. It is therefore critical to assess renal function before contrast administration and implement hydration protocols as needed. Despite these concerns, the radiotracers used in the PET component, such as [18F]-FDG, generally do not produce significant adverse effects. Mild reactions such as localized pain at the injection site, transient warmth, or nausea are infrequent and self-limiting, making PET radiotracers overall well-tolerated by patients [49].

Patient Safety:

Patient safety also encompasses the management of radiation exposure. PET-CT involves ionizing radiation from both the radiotracer and the CT scan. The PET component alone typically delivers approximately 7.5 millisieverts (mSv), while the combined PET-CT scan results in higher cumulative doses, ranging from 14 to 30 mSv depending on the specific CT parameters and protocol used. This exposure, although within acceptable diagnostic ranges, necessitates caution in sensitive populations. Radiation poses particular risks during pregnancy, as ionizing radiation can adversely affect fetal development. In such cases, alternative imaging modalities should be considered whenever feasible. For breastfeeding women, radiation safety recommendations advise minimizing close contact with infants or pregnant women for up to 12 hours post-scan. Additionally, breast milk should be expressed and discarded during this period, with breastfeeding safely resuming after approximately 24 hours. Techniques such as using half-dose radiotracers have demonstrated the ability to maintain diagnostic image quality while reducing radiation exposure, offering a safer approach for vulnerable populations [49].

Clinical Significance:

From a clinical perspective, understanding these potential complications is essential for optimizing patient care. PET-CT's safety profile, combined with its high diagnostic accuracy, makes it a critical tool across multiple medical specialties. Clinicians must provide comprehensive pre-scan education, including guidance on dietary restrictions, avoidance of strenuous exercise, and management of medications, to minimize confounding factors that may affect imaging quality. Awareness of possible allergic reactions and renal complications allows timely intervention, while careful consideration of radiation exposure ensures patient safety in high-risk groups [50]. The clinical significance of PET-CT continues to expand. Its applications in oncology, including tumor detection, staging, and therapy monitoring, are well-established, while emerging uses in neurology, cardiology, psychiatry, and immunology demonstrate their growing versatility. PET-CT's ability to provide functional, metabolic, and molecular insights into disease processes has transformed diagnostic strategies and patient management. New applications continue to emerge, emphasizing PET-CT's evolving role as a vital radiological tool with substantial diagnostic, prognostic, and therapeutic value. By balancing the benefits of detailed functional imaging with careful attention to potential complications and radiation safety, PET-CT can be employed effectively and safely across diverse clinical contexts [50].

Conclusion:

In conclusion, Positron Emission Tomography (PET) stands as a pivotal diagnostic modality that has fundamentally transformed modern medical imaging. Its unique capacity to provide quantitative, functional, and molecular data offers an unparalleled view into cellular metabolism and disease pathophysiology, far exceeding the capabilities of purely anatomical techniques. The clinical utility of PET, particularly when integrated with CT, is firmly established across a vast spectrum of fields, from its foundational role in oncology for staging and monitoring treatment response to its critical applications in neurology for differentiating dementias and localizing seizure foci, and in cardiology for assessing myocardial viability. The continuous development of novel, targeted radiotracers, such as 68Ga-DOTA peptides and FAPI, is further broadening its scope, enhancing diagnostic precision, and paving the way for theranostic applications. For radiologists, a comprehensive understanding of PET principles, indications, and potential interfering factors is essential to maximize its diagnostic yield and ensure patient safety. As technology and radiopharmaceuticals advance, PET imaging is poised to remain at the forefront of precision medicine, enabling increasingly personalized and effective patient care.

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تصوير البوزيترون المقطعي: مراجعة محدثة لأطباء الأشعة

الملخص:

خلفية: يُعد تصوير البوزيترون المقطعي (PET) أحد الركائز الأساسية للتصوير الوظيفي والجزيئي، حيث يتيح تصور العمليات الأيضية والفسيولوجية داخل الجسم الحي. يستخدم هذا التصوير نظائر مشعة تتراكم في الأنسجة ذات النشاط الكيميائي الحيوي العالي، مقدمة معلومات حاسمة تتجاوز ما توفره الصور التشريحية.

الهدف: تهدف هذه المراجعة المحدثة إلى تجميع التطبيقات الحالية لمفهومPET ، المبادئ التكنولوجية، والأهمية السريرية لهذا التصوير لأطباء الأشعة، مع التركيز على فائدته في مختلف التخصصات الطبية وظهور نظائر مشعة جديدة.

الطرق: توحد هذه المراجعة الأدلة المتعلقة بإجراءاتPET ، بما في ذلك طرق إعطاء النظائر المشعة، بروتوكولات التصوير، ودمج PET مع التصوير المقطعي المحوسب .(PET-CT) كما تقيم استخدام النظائر المختلفة، وأهمها F-FDG 18لقياس استقلاب الجلوكوز، ببتيدات Ga-68 DOTAللأورام العصبية الصماوية، والنظائر المتخصصة في علم الأعصاب وأمراض القلب، عبر طيف واسع من الأمراض.

النتائج: يظهر تصوير PET قيمة تشخيصية وتنبؤية عالية. في علم الأورام، يعتبر ضرورياً لتحديد مرحلة الورم، تقييم الاستجابة للعلاج، واكتشاف الانتكاسات. في علم الأعصاب، يساعد في التفريق بين أشكال الخرف وتحديد بؤر الصرع. في أمراض القلب، يقيم بشكل دقيق حيوية عضلة القلب. النظائر الناشئة، مثل FAPI لاستهداف الأرومات الليفية المرتبطة بالسرطان، توسع الإمكانات التشخيصية والعلاجية لهذا التصوير. من الاعتبارات الأساسية إدارة العوامل المؤثرة مثل نظام المريض الغذائي والأدوية لضمان دقة الصور.

الخلاصة: يعد تصوير PET تقنية قوية ومتعددة الاستخدامات أحدثت ثورة في التشخيص الطبي. قدرته على تقديم بيانات جزيئية كمية تجعله أساسياً في الطب الدقيق، موجهًا التشخيص، تخطيط العلاج، ومتابعة الاستجابة العلاجية عبر مجالات سريرية متعددة.

الكلمات المفتاحية: تصوير البوزيترون المقطعي(PET) ، النظائر المشعة، F-FDG18، التصوير الجزيئي، PET-CT، علم الأورام، علم الأعصاب، العلاج التشخيصي.(Theranostics)