Current Applications and Advancements of State-of-the-Art technology of PET-CT

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ABSTRACT

Positron Emission Tomography-Computed Tomography (PET-CT) is an innovative hybrid imaging technique that effectively combines functional and anatomical imaging. This integration enhances the diagnosis and treatment of a wide range of diseases, proving to be particularly valuable in fields such as oncology, neurology, cardiology, and infectious disease management. By offering detailed insights into disease mechanisms, progression, and responses to therapy, PET-CT plays a crucial role in advancing patient care. The continued development of PET-CT incorporates cutting-edge techniques, including the use of novel radiotracers, hybrid imaging modalities, and artificial intelligence (AI)-based image analysis. This review aims to spotlight the technological advancements, emerging trends, application in research, clinical applications, and challenges associated with PET-CT while emphasizing its potential in personalized medicine and the ongoing integration of novel radiotracers and AI technologies. Despite certain limitations, PET-CT is a vital component of modern medical imaging, significantly contributing to the evolution of precision healthcare.

Keywords: PET-CT, hybrid imaging, research applications, clinical applications, deep learning

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INTRODUCTION

The field of medical imaging is advancing at an impressive rate, particularly with the recent integration of molecular information from Positron Emission Tomography (PET) and the anatomical details provided by Computed Tomography (CT). These developments are enhancing diagnostic capabilities and improving patient outcomes. PET and CT are two fundamental imaging techniques that, when combined, offer a unique and powerful diagnostic tool. PET provides functional information based on metabolic activity, typically using radiolabeled glucose analogs such as ^{18}F-fluorodeoxyglucose (FDG), while CT offers high-resolution anatomical images based on X-rays. The combination of PET and CT allows for precise localization of functional abnormalities in anatomical structures, providing superior accuracy in diagnosing and monitoring diseases. The early clinical applications of Positron Emission Tomography (PET) emerged in neurology and cardiology during the 1980s, followed by its adoption in oncology in the 1990s. In the late 1990s, ^{18}F-FDG was widely utilized as the radiopharmaceutical for the evaluation of oncology patients. The clinical use of PET received a significant enhancement in 1998 when health care agencies in the United States approved reimbursement for PET scanning (1-3). As the PET-CT has been increasingly used in research and clinical investigations, it is necessary to summarize its clinical applications, with the aim of providing a reference for researchers and pointing out its future directions. This review discusses the wide range of applications of PET-CT in clinical practice, application in research, the recent advances in imaging technologies, and the integration of artificial intelligence and new radiotracers. Furthermore, we highlight the future directions of PET-CT, including its potential in personalized medicine and other emerging medical fields.

PRINCIPLES OF PET-CT TECHNOLOGY

Positron Emission Tomography (PET) imaging is a powerful diagnostic tool that provides insight into the metabolic processes within the body. The technique involves the use of positron-emitting radiotracers, which are compounds that emit positrons after being introduced into the bloodstream. Once injected, these radiotracers travel to specific tissues or organs, where they participate in biological processes. When a positron encounters an electron within the body, they annihilate each other, producing gamma of 511 KeV rays moving in opposite directions (4). PET scanners are equipped with advanced detectors that capture these gamma rays and utilize sophisticated algorithms to reconstruct detailed three-dimensional (3D) images. These images reveal the distribution and concentration of the radiotracer, reflecting the metabolic activity of the tissues, which can help identify abnormalities or disease states.

CT scanners use X-ray beams to capture cross-sectional images of anatomical structures, providing detailed visualizations of organs, tissues, and bone. These images are processed to create comprehensive three-dimensional representations, enhancing clinicians' ability to accurately evaluate medical conditions.

PET and CT imaging technologies have been combined into a single, advanced imaging system known as hybrid (1). This hybrid approach facilitates simultaneous functional and anatomical imaging, meaning that while CT provides detailed structural information, PET offers insights into metabolic activity and physiological function. The fusion of these two imaging modalities significantly improves the accuracy of detecting and delineating lesions, as it provides complementary information that can be critical for diagnosis. Consequently, healthcare professionals are equipped with enhanced tools for treatment planning, enabling more informed decisions regarding patient care and management. All recent PET-CT scanners operate in 3D mode, without inter-plane septa. Time-of-flight positron emission tomography (ToF-PET) has re-emerged and matured over the last decade and improved the capabilities of PET imaging. Regarding image quality and overall effective sensitivity, ToF-PET has demonstrated notable advantages over traditional PET. In 3D mode, coincident photons are detected in all directions, which allows for greater photon sensitivity than imaging in traditional 2D mode, at the expense of increased scatter. The principle of PET-CT imaging is illustrated in Figure 1 (2-4).

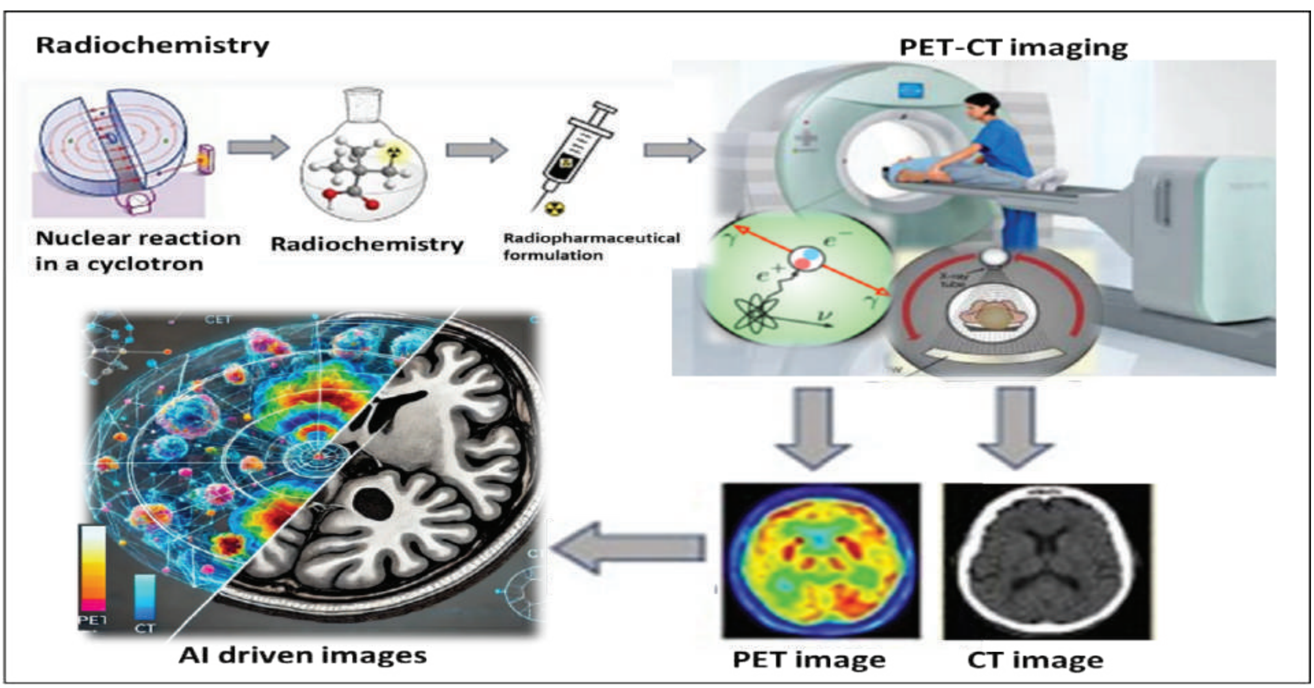

Figure 1: An illustration of the principles of PET-CT imaging

PET- TRACERS

A PET radiotracer (also known as PET tracer) is a positron-emitting radiopharmaceutical used in positron emission tomography (PET). Each tracer consists of a positron-emitting isotope (radioactive tag) bound to an organic ligand (targeting agent). The ligand component of each tracer interacts with a protein target, resulting in a characteristic distribution of the tracer throughout the tissues. There is an increasing list of chemical compounds which are being used for PET imaging. A list of commonly used compounds, with their radioactive isotope in parentheses, includes: PET imaging has been performed using a variety of positron-emitting radio-isotopes (Table 1). The first four isotopes listed in Table 1, are significant because they can all be easily added to biological compounds to create useful bio-tracers (5).

Table 1: Common PET Radiotracers for imaging patients

Isotope	Half life	Positron energy (MeV)	Positron range (mm)	Compounds	Production source
^{11}C	20 minutes	0.385	1.1	acetate (^{11}C) choline (^{11}C)	Cyclotron
^{13}N	10 minutes	0.492	1.4	ammonia (^{13}N)	Cyclotron
^{15}O	2 minutes	0.735	1.5	oxygen-15 labeled water	Cyclotron
^{18}F	110 minutes	0.250	1.0	fludeoxyglucose (^{18}F) sodium fluoride (^{18}F) fluoro-ethyl-spiperone (^{18}F) FDOPA (^{18}F) FDDNP (^{18}F)	Cyclotron
^{64}Cu	10 minutes	0.278	0.69	^{64}Cu to a chelating agent like DOTA	Reactor or Cyclotron
^{68}Ga	67.7 minutes	0.836, 0.352	2.9	(PSMA) (^{68}Ga) DOTATOC, DOTANOC, DOTATATE (^{68}Ga)	Generator
^{82}Rb	1.27 minutes	1.55	7.49	rubidium (^{82}Rb) chloride	Generator

Among the various radiotracers utilized in PET imaging, 18F-FDG stands out as the most widely used. This radiotracer is a glucose analog, which means it mimics glucose and is taken up preferentially by tissues with high metabolic activity, such as cancer cells. However, ongoing research and technological advancements have led to the development of a diverse array of novel radiotracers that target specific diseases or metabolic pathways. These innovations aim to improve the diagnostic accuracy of PET. ^{11}C-methionine and amino acid, has shown great promise in evaluating brain tumors and other cancers. ^{11}C-choline and ^{11}C-acetate have been used in prostate cancer to evaluate the primary and metastatic disease. 13N-labelled ammonia is another PET tracer used for myocardial perfusion studies. ^{82}Rb is a potassium analog and is used as a first pass extraction agent to assess myocardial perfusion in the same way as 201Th or ^{99m}Tclabelled compounds imaging, allowing for better differentiation between healthy and diseased tissues, and enhancing both specificity and sensitivity in medical imaging (5).

APPLICATIONS OF PET-CT

a) Research

There are a lot of potential applications of hybrid PET-CT imaging systems. PET-CT imaging is currently used mostly to study tumors, nervous system diseases, cardiovascular diseases, and systemic immune diseases (6). Due to radiation exposure, traditional PET-CT examination is generally used in the detection of tumors, and is not recommended for healthy individuals. However, the low-dose and ultra-low-dose imaging enabled by the whole-body PET-CT systems have advanced the exploration of PET imaging in healthy individuals for the research (7). The highly sensitive PET scanner enables a decrease in the dose of radiopharmaceuticals administered, without compromising image quality. A healthy male subject experienced an intravenous injection of ^{18}F-FDG with a dose of 1.85 MBq/kg, and reconstructed dynamic PET images of the first three minutes, 150–153 minutes, and 300–303 minutes were taken [Figure 2(a)] (8). The sensitivity of long a FOV enables whole-body PET scanners to generate diagnostic images while reducing scan time. The reconstruction images of an ultrafast PET scan were done on a 64-year-old woman with hepatocellular carcinoma using 2 iterations and a 45-second acquisition [Figure 2(b)] (9). The increased sensitivity of the PET allows a reduced dose of the injected radiopharmaceuticals while maintaining acceptable image quality. The complete image and axial view of the series of dose-reduced images depict a micro-lesion in the subcapsular area of the liver in a 3-year-old patient diagnosed with Burkitt Lymphoma. This micro-lesion is identical in all dose-reduction images [Figure (2c)] (10). A dynamic scan at delayed time is obtained following the injection of 496 MBq of 18F-FDG in a patient with metastatic colon cancer reconstruction for 10 minutes at 4.2 hours post-injection [Figure 2(d)] (11).

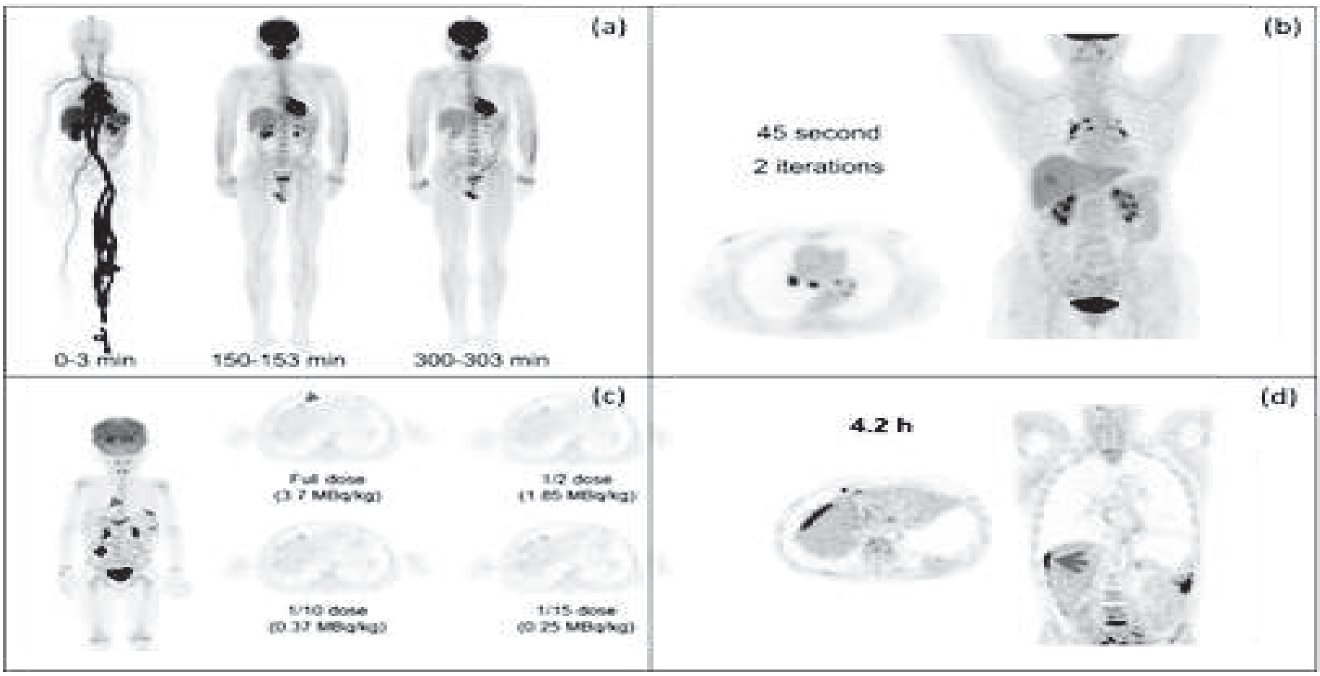

Figure 2: (a) dynamic PET-CT images of healthy volunteers, (b) ultrafast imaging, (c) low-dose imaging and (d) delayed imaging.

b) Clinical applications

PET-CT systems have revolutionized cancer detection, staging malignant lesions, and evaluating therapeutic responses. They visualize metabolic activity in tissues, enabling earlier detection and accurate staging of tumors. PET-CT aids in treatment planning, optimizing radiation targeting while sparing healthy tissue. It also monitors patients undergoing chemotherapy, radiation therapy, or immunotherapy, detecting changes in metabolic activity and detecting cancer recurrence. Unlike conventional imaging, PET-CT differentiates between viable tumors and post-treatment changes.

PET-CT is widely used in the diagnosis and management of neurological disorders such as Alzheimer’s disease, Parkinson’s disease and Huntington’s disease (13). It reveals reduced glucose metabolism patterns in brain regions, aiding early diagnosis and disease progression. 18F-florbetapir is used for Alzheimer's diagnosis and localizing seizure foci in refractory epilepsy, aiding surgical planning (14).

PET-CT is a vital tool for detecting tumor recurrence, radiation-induced changes in brain tumors, and assessing tumor grade. It also evaluates myocardial viability, particularly in patients with coronary artery disease, identifying viable areas for revascularization and intervention (15). PET-CT is invaluable in identifying infections, particularly in cases where conventional imaging is insufficient. It is useful for detecting bone infections, endocarditis, and other deep-seated infections that may not show up on CT alone (16). PET-CT is used to monitor chronic inflammatory conditions such as sarcoidosis, vasculitis, and inflammatory bowel disease (IBD) (17). As shown in Figure 3, PET-CT is used in a variety of clinical applications for different organs (18, 19).

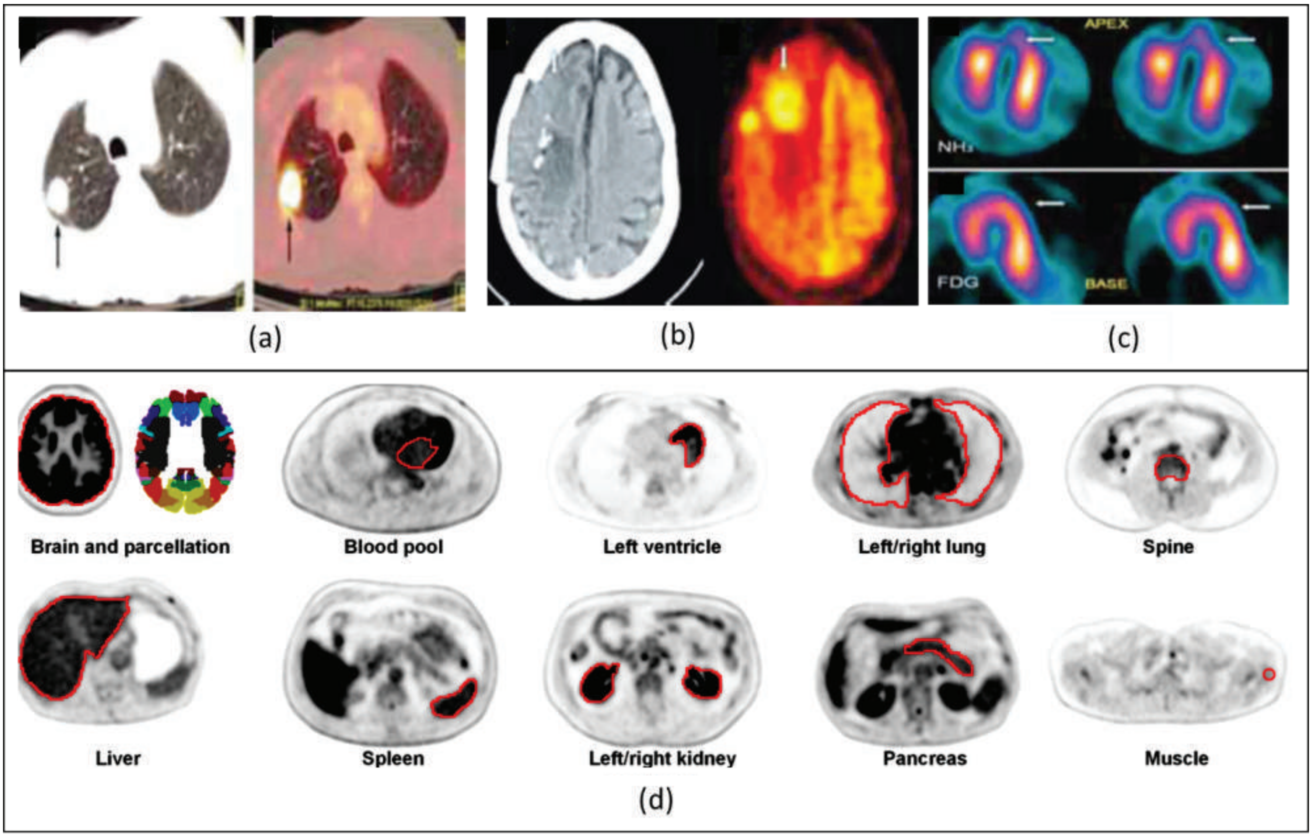

Figure 3: (a) FDG PET/CT scan for solitary pulmonary nodule, (b) Brain FDG PET/CT scan in an operated, post radiotherapy case of high-grade glioma, (c) Cardiac PET/CT can, horizontal long axis sections of the left ventricle, (d) Schematic diagram of the systemic metabolism network constructed SUV images of 11 organs regions.

RECENT ADVANCEMENTS IN PET-CT

PEM dedicated to Breast Imaging

Commercially available whole-body PET systems with relatively low spatial resolution limits to detect small lesions uptake in smaller lesions that are prevalent in early-stage breast cancer. Positron emission mammography (PEM) has been developed to address the shortcomings of WB PET and has demonstrated encouraging potential in the detection of breast cancer (20). PEM has the same mechanism as PET. Among the many benefits of the PEM system are its high sensitivity and good spatial resolution, both of which help to lower the radionuclide dose and speed up acquisition. The researcher also used high resolution dual-head PET/PEM verifying the range of protons beam in the proton therapy.

PET with Semiconductor Detectors

For higher stopping power with better energy resolution than the conventional scintillation detectors currently semiconductors are used in PET scanners (21-22). Semiconductor PET detectors are a promising technology for positron-emission tomography (PET) scanners that could lead to higher-resolution images with less scatter noise and superior individual readout. For example, a new generation of time-of-flight PET scanners (TOF-PET) are increasingly using silicon photomultipliers (SiPMs) as their preferred photodetectors.

Novel Radiotracers

The development of new radiotracers targeting specific cellular processes has broadened the applications of PET-CT in oncology, neurology, and cardiology (23). New tracers target specific tumor biomarkers, allowing for more personalized and targeted imaging. Radiotracers for neurodegenerative diseases and infection are also showing promising results. Radiotracers such as ^{18}F-FDOPA for Parkinson's disease imaging, ^{18F}-FLT for tumor proliferation and ^{18}F-florbetapir have enhanced the specificity and sensitivity of PET scans.

PET-MRI Hybrid Imaging Modalities

Recently, vendors introduced hybrid PET-MRI imaging modalities, which combines the functional imaging of PET with the superior soft tissue contrast of Magnetic resonance imaging (MRI) (24). This technique is especially useful in neurology and oncology. Nevertheless, these systems could potentially be used for cardiac imaging PET-MRI can also be superior in depiction of the myocardial viability/hibernation and in assessing stem-cell and gene therapies.

Artificial Intelligence (AI) and Machine Learning

AI-based algorithms are being developed to enhance the accuracy of PET-CT image interpretation (25). AI can help in automating tasks like lesion detection, classification, and quantification, making the process faster and more reliable. The combination of the PET-CT imaging with machine learning techniques, especially deep learning, may have the potential to solve practical problems that exist in current applications. Since analytical reconstruction methods may generate images with a high level of noise and iterative methods are time-consuming for PET-CT image reconstruction, deep learning-based methods have solved those constraints.

CONCLUSION

PET-CT is a vital tool in modern medicine, providing non-invasive insights into disease biology, improving patient outcomes, and supporting precision medicine. Its broad applications include oncology, neurology, cardiology, and infectious diseases. Future developments include novel radiotracers, hybrid imaging modalities, and AI integration.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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