# AI Techniques in PET Medical Imaging: A Survey

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## Abstract

The integration of artificial intelligence (AI) into positron emission tomography (PET) imaging has significantly transformed the field, enhancing image reconstruction and diagnostic accuracy. This survey paper explores the application of AI techniques, particularly generative models, deterministic methods, and neural networks, in PET imaging. AI advancements have addressed challenges such as low resolution and high noise, improving image quality and diagnostic outcomes. Generative adversarial networks (GANs) and diffusion models have been pivotal in image synthesis, enabling the creation of high-quality synthetic PET images and enhancing cross-modal synthesis with modalities like MRI. Deterministic methods, when integrated with AI, have refined reconstruction processes, improving both image clarity and computational efficiency. The survey highlights the transformative impact of AI in PET imaging, emphasizing its role in improving diagnostic workflows and patient outcomes. Challenges such as data availability, computational costs, and model generalization are discussed, alongside innovations addressing these issues. The paper also considers ethical and regulatory considerations, advocating for explainable AI models to ensure clinical acceptance. Ultimately, the survey underscores AI's potential to revolutionize PET imaging, promising significant advancements in diagnostic accuracy and efficiency.

## 1 Introduction

### 1.1 Significance of AI in PET Imaging

The integration of artificial intelligence (AI) into positron emission tomography (PET) imaging has significantly transformed the field, enhancing diagnostic accuracy and efficiency. AI techniques, particularly deep learning, effectively address challenges such as low resolution and high noise, leading to improved image quality and diagnostic outcomes [1]. The development of explainable deep learning models further emphasizes the importance of transparency and interpretability in AI-driven diagnostic systems, which are crucial for clinical adoption [2].

AI advancements have markedly improved the synthesis of high-quality PET images from various modalities, including structural magnetic resonance imaging (sMRI). By leveraging the strengths of these imaging techniques, AI enhances diagnostic accuracy, facilitates rapid imaging protocols, and reduces radiation exposure, ultimately improving patient comfort and clinical outcomes. This integration streamlines the PET imaging workflow and addresses the complexities of modern imaging systems [3, 4, 5, 6]. Moreover, the incorporation of Time-of-Flight (TOF) information further refines image properties, underscoring AI's role in enhancing diagnostic precision.

AI methods are particularly effective in improving PET image quality, especially when reconstructing images from ultra-low-dose data. Advanced algorithms reduce noise while maintaining high resolution and preserving anatomical details. Techniques like deep learning-based image denoising and deblurring utilize sophisticated architectures to enhance spatial resolution and contrast recovery, addressing common PET imaging challenges. The integration of AI not only optimizes image quality but also supports low-dose imaging protocols, enhancing diagnostic capabilities and patient comfort

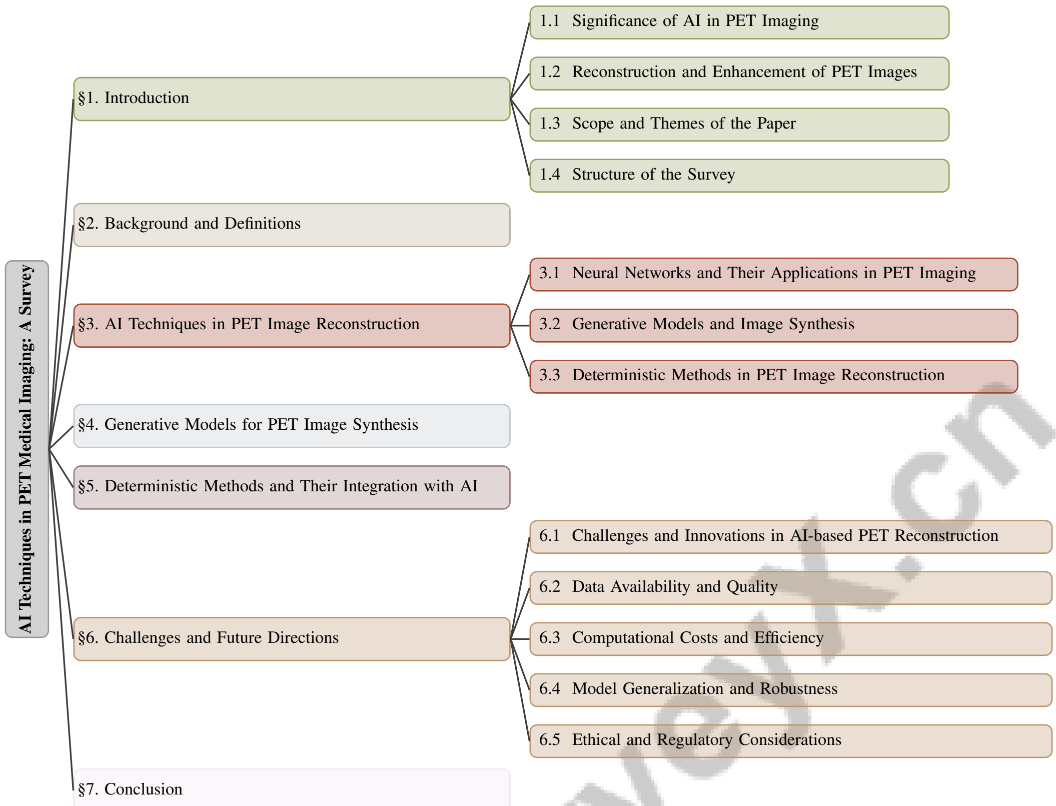



Figure 1: chapter structure

[6, 7, 3, 8, 9]. Generative adversarial networks (GANs) have also significantly advanced image quality and reconstruction efficiency, highlighting their impact in medical imaging contexts.

The development of scalable motion correction algorithms illustrates AI's profound impact on PET imaging, enhancing image reconstruction quality by addressing high noise levels and low spatial resolution. By employing AI techniques for image denoising and deblurring, researchers significantly improve the qualitative and quantitative aspects of PET imaging. This integration not only enhances PET workflow efficiency but also opens new avenues for clinical applications, particularly in Total-Body PET systems, which offer superior sensitivity and diagnostic capabilities [3, 6]. Additionally, AI provides non-invasive and cost-effective imaging alternatives, addressing the limitations of PET due to its radioactive nature and cost. Collectively, these advancements underscore AI's transformative impact on PET imaging, offering substantial improvements in diagnostic workflows and patient outcomes, particularly in early diagnosis of neurological disorders through precise segmentation of PET scan images.



### 1.2 Reconstruction and Enhancement of PET Images

Artificial intelligence has profoundly influenced the reconstruction and enhancement of PET images, effectively addressing challenges such as low spatial resolution and high noise levels. AI techniques have refined image reconstruction workflows, enhancing diagnostic accuracy and efficiency [10]. For instance, methods like LMPDNet improve the reconstruction quality and efficiency of TOF-PET imaging, underscoring AI's critical role in enhancing image clarity [11].

Advanced AI methodologies, such as PCSA-GAN, utilize pyramid convolution and attention mechanisms to elevate PET image quality, demonstrating the potential of cross-modal medical image generation for enhanced reconstruction [12]. The STPDnet approach effectively models spatial and temporal correlations, further improving PET image quality and clarity [13].

Deep learning methods are instrumental in predicting standard-dose images from low-dose data, maintaining high diagnostic standards while ensuring safer imaging practices [14]. The challenge of accurate attenuation correction in PET/MRI, due to the lack of direct correlation between MR image intensities and attenuation coefficients, highlights the importance of AI in enhancing PET image reconstruction [15]. Jahangir et al. address deep learning-based attenuation and scatter correction in the image domain, advancing hybrid PET/MRI systems [16].

AI enhances PET images through end-to-end deep learning pipelines that incorporate a 3D U-Net for segmentation and a recurrent neural network for deriving a model-corrected blood input function, improving reconstruction quality [17]. Learned convolutional regularizers also enhance PET image quality, particularly in low-count quantitative PET scenarios [18]. Automating complex tasks, such as the registration of coronary 18 F-sodium-fluoride PET to CT angiography, further demonstrates AI's capacity to enhance image clarity and quality [19]. The integration of a penalized-likelihood framework with 3D convolutional sparse coding enhances PET image quality while minimizing computational costs [1].

These advancements collectively illustrate AI's transformative impact on PET image reconstruction, offering significant improvements in diagnostic workflows and patient outcomes through superior image quality and clarity [20].

### 1.3 Scope and Themes of the Paper

This survey explores the integration of AI techniques in PET imaging, focusing on the transformative roles of generative models, deterministic methods, and neural networks in enhancing diagnostic accuracy and efficiency. A central theme is the application of generative models, such as GANs, which have significantly advanced medical imaging through improved image synthesis and registration processes [19]. Techniques like fully convolutional networks and conditional GANs highlight the potential of deep learning in developing virtual PET imaging methods using CT scans, showcasing AI's contribution to enhanced image synthesis [1].

The survey emphasizes the integration of deep learning techniques for image-to-image translation and MRI reconstruction, with convolutional neural networks (CNNs) and GANs playing pivotal roles. These methods are crucial for addressing challenges in low-dose PET imaging, as demonstrated by strategies utilizing multiple low-dose images for enhanced reconstruction [16]. Additionally, the development of multi-hypothesis deep learning frameworks for generating plausible pCT representations underscores the importance of minimizing PET reconstruction errors.

Deterministic methods are explored through model-based image reconstruction (MBIR) techniques, such as learned regularization and anatomical priors in penalized-likelihood PET image reconstruction [1]. The integration of 3D U-Net and recurrent neural networks (RNNs) further demonstrates the potential of deep learning in refining PET image analysis and reconstruction. This survey provides a comprehensive review of deep learning methods applied to PET image reconstruction, focusing on enhancing image quality and diagnostic workflows.

Moreover, the survey acknowledges broader applications of AI in healthcare, including ethical considerations, legal frameworks, and algorithmic challenges, essential for the responsible deployment of AI technologies in clinical settings [2]. Through examining these themes, this paper offers a robust framework for understanding the current landscape and future directions of AI in PET imaging, ultimately aiming to revolutionize diagnostic workflows and improve patient outcomes.

### 1.4 Structure of the Survey

This survey is structured to provide a comprehensive exploration of AI techniques in PET imaging. It begins with an **Introduction** section that underscores the significance of AI in enhancing PET imaging, focusing on the transformative roles played by generative models, deterministic methods, and neural networks. The introduction sets the stage for the detailed discussions that follow by highlighting the key themes and scope of the paper.

The next section, **Background and Definitions**, offers foundational insights into PET imaging and essential AI concepts relevant to this field. It provides an overview of the principles of PET and defines critical terms such as generative models, deterministic methods, and neural networks, establishing a baseline understanding for readers.

Following this, the survey delves into **AI Techniques in PET Image Reconstruction**, examining various AI methodologies employed to improve PET image quality and reconstruction speed. This section is subdivided into discussions on neural networks, generative models, and deterministic methods, each highlighting their specific contributions and applications in PET imaging.

The discussion advances to **Generative Models for PET Image Synthesis**, which delves into the application of advanced generative models, such as GANs and diffusion models, for creating synthetic PET images. These models enhance the quality and resolution of synthesized images and address challenges in medical imaging, such as data scarcity and the need for high-quality training datasets for computer-aided diagnosis systems. By leveraging high-level semantic features and incorporating multi-modality inputs, these generative approaches significantly improve diagnostic accuracy and operational efficiency in clinical settings [21, 22, 23, 24].

Subsequently, the survey addresses **Deterministic Methods and Their Integration with AI**, focusing on how deterministic approaches can be combined with AI to further improve image reconstruction and synthesis. This section includes examples of successful integrations in clinical settings and discusses hybrid and multi-modal approaches for enhanced imaging.

The penultimate section, **Challenges and Future Directions**, identifies current obstacles in AI-based PET imaging, such as data availability, computational costs, and model generalization. It also discusses potential future advancements and innovations in AI techniques.

In conclusion, the paper encapsulates the pivotal discussions surrounding the transformative impact of AI on PET imaging, particularly with the advent of Total-Body PET (TB-PET) systems. It emphasizes AI's potential to enhance diagnostic workflows through improved image acquisition and data analysis, leading to quicker imaging, reduced radiation exposure, and better patient comfort. The review also highlights the necessity for collaboration in the medical imaging field to fully leverage the synergy between AI and TB-PET, addressing industry-specific challenges and advocating for shared resources and open-source initiatives to maximize the technology's capabilities and improve patient outcomes [10, 6].The following sections are organized as shown in Figure 1.

## 2 Background and Definitions

### 2.1 Overview of Positron Emission Tomography (PET)

Positron Emission Tomography (PET) is a pivotal imaging technique in medical diagnostics, renowned for its ability to visualize physiological and biochemical processes with high sensitivity and specificity. It involves the administration of radiotracers tagged with positron-emitting isotopes, which decay and emit positrons that interact with electrons, resulting in gamma photon emission. These photons are detected by the PET scanner, facilitating the reconstruction of detailed images that accurately represent the spatial distribution of the radiotracer within the body [20]. PET's capability to detect abnormal glucose metabolism is crucial in oncology for tumor identification [25], and it plays a significant role in diagnosing neurological disorders and evaluating treatment responses [26].

The integration of PET with computed tomography (CT) in PET/CT systems enhances diagnostic precision by providing complementary anatomical information, though it also increases radiation exposure, necessitating rigorous patient safety protocols [27]. Accurate image reconstruction in these systems depends on the precise alignment of functional and anatomical images, typically achieved through affine registration techniques [28]. However, PET imaging faces challenges due to the ill-posed nature of reconstructing images from noisy sinogram data and Poisson noise, complicating the acquisition of high-quality datasets [10].

Dynamic PET imaging expands the modality's utility by reconstructing temporal series of spatial concentration distributions from noisy sinograms, offering insights into tracer kinetics crucial for early disease detection and monitoring, particularly in Alzheimer's Disease [29]. The limited use of dynamic 2-[18F] fluoro-2-deoxy-D-glucose PET, primarily due to its reliance on invasive arterial blood sampling for quantitative analysis, underscores the need for non-invasive alternatives [17].

Challenges persist in synthesizing accurate pseudo-CT images from MRI data for attenuation correction [15] and efficiently reconstructing high-quality, motion-corrected direct Patlak images from dynamic PET scans [30]. Attenuation and scatter correction are critical for quantitative PET imaging, especially in hybrid systems lacking anatomical imaging [16]. Despite these challenges, advancements in imaging techniques and data analysis continue to enhance PET's clinical utility, solidifying its role as a cornerstone in modern diagnostics, as evidenced by its application in evaluating lymphoma subtypes such as DLBCL and PMBCL [31].

### 2.2 Key Concepts in AI for Medical Imaging

The incorporation of artificial intelligence (AI) into medical imaging, particularly in Positron Emission Tomography (PET), involves crucial concepts that significantly enhance image reconstruction and analysis. Deep learning techniques, encompassing both model-based and data-driven approaches, are essential for improving PET image resolution and reducing noise, thereby enabling more precise diagnostics [20]. Generative Adversarial Networks (GANs) are instrumental in generating pseudo-CT images from non-attenuation corrected PET data, crucial for accurate attenuation correction without additional anatomical imaging.

Medical image segmentation and clustering are fundamental for precise PET image analysis, with symmetry-based techniques providing robust frameworks for enhancing image quality [32]. These methods are complemented by evaluation frameworks that incorporate traditional segmentation metrics alongside clinically relevant lesion measures, ensuring AI-driven enhancements meet clinical needs [31].

AI in medical imaging also addresses significant challenges, such as data biases, the need for robust regulatory frameworks, and the ethical implications of AI-generated medical decisions [33]. The black-box nature of deep learning algorithms presents a core issue, hindering clinical adoption due to a lack of transparency in decision-making processes [2]. This highlights the necessity for developing explainable AI models to ensure transparency and facilitate clinical acceptance.

These concepts collectively underscore AI's transformative impact on medical imaging, particularly in enhancing PET image reconstruction and diagnostics. By addressing both technical and ethical challenges, AI is advancing diagnostic capabilities and fostering innovative solutions. Deep learning techniques are vital in improving image analysis and interpretation while tackling critical issues such as data privacy, algorithmic bias, and the need for robust regulatory frameworks. As AI technologies, including generative AI and large-scale models, continue to evolve, they promise to enhance clinical workflows, increase diagnostic accuracy, and ultimately transform patient care in the medical imaging landscape [34, 35, 6, 33, 20].

## 3 AI Techniques in PET Image Reconstruction

### 3.1 Neural Networks and Their Applications in PET Imaging

Neural networks have revolutionized Positron Emission Tomography (PET) imaging by enhancing image reconstruction and analysis, thereby improving image quality and diagnostic precision. Convolutional Neural Networks (CNNs), particularly architectures like U-Net, play a crucial role in PET image segmentation and reconstruction, as demonstrated by evaluations of frameworks such as UNet, SegResNet, DynUNet, and SwinUNETR [31]. These advancements extend to automatic segmentation of internal carotid arteries, thereby refining PET reconstruction accuracy [17].

Innovative frameworks like BCD-Net utilize learned convolutional regularizers for model-based reconstruction in low-count PET scenarios, addressing challenges associated with low-count imaging and enhancing diagnostic performance [18, 20]. The Symmetry Based Cluster Approach (SBCA) further enhances segmentation accuracy by employing symmetry-based distances in PET scans [32].

Neural networks facilitate direct application of deep learning techniques to PET images, improving reconstruction and analysis [16]. The integration of 3D structural information without extensive training data exemplifies their utility in advancing image quality [1]. AI, including neural networks, enhances detection and classification tasks, leading to improved diagnostic accuracy in PET imaging [25]. These advancements underscore the transformative impact of neural networks on PET imaging, promising further enhancements in diagnostic workflows and patient outcomes.

Figure 2 illustrates the hierarchical categorization of neural network applications in PET imaging, focusing on image reconstruction, image segmentation, and diagnostic applications. Each category highlights specific neural network models and methodologies that contribute to advancements in PET imaging techniques. The first figure shows a convolutional neural network (CNN) architecture, specifically a U-Net, which employs convolutional layers to downsample input feature maps for accurate image reconstruction. The second figure highlights the iterative nature of model training to optimize parameters, followed by performance evaluation. The third figure compares blood and tumor activity in MRI scans, showcasing dynamic changes in blood activity over time. These examples demonstrate the transformative potential of neural networks in advancing PET imaging [36, 3, 37].

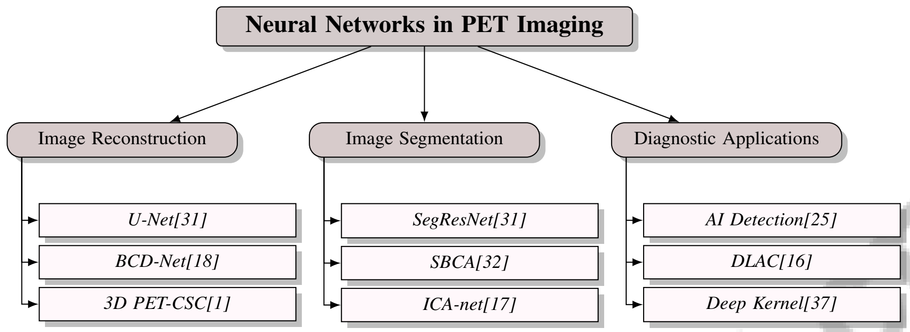



Figure 2: This figure illustrates the hierarchical categorization of neural network applications in PET imaging, focusing on image reconstruction, image segmentation, and diagnostic applications. Each category highlights specific neural network models and methodologies that contribute to advancements in PET imaging techniques.

### 3.2 Generative Models and Image Synthesis

Generative models, particularly Generative Adversarial Networks (GANs) and diffusion models, have significantly advanced the synthesis of Positron Emission Tomography (PET) images, addressing challenges related to low-dose imaging and enhancing diagnostic quality. GANs, such as the Virtual PET Estimation (VPET) method, utilize conditional GANs to generate PET-like images from CT scans, enhancing diagnostic workflows [38]. Their application in image-to-image translation and MRI reconstruction improves robustness and accuracy in data-scarce scenarios [39].

GANs also facilitate the creation of pseudo-CT images for automated registration processes, thereby improving PET image reconstruction [19]. Advanced models like DUAL-GLOW leverage MRI-PET relationships to synthesize PET images, showcasing the capabilities of generative modeling techniques in medical imaging.

Diffusion models have emerged as alternatives to traditional GANs for PET image synthesis, offering enhanced stability and computational efficiency while producing higher-quality images with improved sample consistency. Studies indicate that diffusion probabilistic models (DPMs) achieve superior log-likelihood scores, enhancing clinical reliability in reconstructed PET images [21, 40, 22]. These models improve the generation quality and diversity of 3D medical images, providing a promising avenue for high-quality image synthesis.

Innovative approaches like ProAmGAN employ a progressive growing strategy to generate high-dimensional images reflecting the statistical properties of medical objects from noisy measurements, illustrating the profound influence of generative models on PET imaging. They significantly enhance image quality and diagnostic accuracy through effective lesion detection and segmentation, facilitating data augmentation and translation of low-dose PET images to full-dose equivalents [41, 21, 23]. By leveraging GANs and diffusion models, the field continues to evolve, promising further enhancements in medical imaging and patient outcomes.

### 3.3 Deterministic Methods in PET Image Reconstruction

Deterministic methods have been pivotal in advancing Positron Emission Tomography (PET) image reconstruction by providing a systematic framework for image synthesis through mathematical modeling. These methods, often reliant on predefined grids, face challenges such as limited resolution and susceptibility to noise. Recent developments, including Gaussian mixture models and score-based generative models, employ robust statistical properties and advanced image distribution modeling to enhance image quality and computational efficiency [42, 43, 44, 45, 46]. Integrating artificial



AI-generated, for reference only.

intelligence (AI) with deterministic methods offers a promising avenue to overcome these limitations, enhancing image synthesis and reconstruction precision.

The integration of deterministic iterative reconstruction techniques with AI, exemplified by the LMPDNet method, employs a learned primal-dual approach to optimize reconstruction, effectively combining deterministic strategies with AI-driven enhancements for superior image quality [11]. Similarly, the STPDnet method enhances image synthesis by modeling spatial and temporal correlations, demonstrating the potential of deterministic methods alongside AI [13].

The Direct PET Image Reconstruction with Deep Image Prior (DIP-PR) method contrasts with conventional deep learning by eliminating the need for pre-reconstructed images during training, representing a novel integration of deterministic principles with AI [47]. This approach underscores the potential of deterministic methods to enhance image synthesis without extensive pre-training datasets.

Deterministic methods have also been integrated with AI to address low signal-to-noise ratio (SNR) challenges in PET imaging. For instance, learned convolutional regularizers in model-based image reconstruction improve image quality in low-count PET scenarios [18]. The SBCA method applies symmetry principles to enhance segmentation processes, illustrating the synergy between deterministic methods and AI in improving PET imaging outcomes [32].

The integration of deterministic methods is exemplified by computing a model-corrected blood input function, which corrects for partial volume and spillover effects, refining image reconstruction [17]. The dual-channel deep learning model incorporating both PET-nonAC and PET-SegAC images highlights the role of deterministic methods in enhancing attenuation correction accuracy [16].

These advancements illustrate the transformative impact of integrating deterministic methods with AI in PET imaging. The advent of Total-Body PET (TB-PET) systems enhances imaging sensitivity and efficiency, enabling rapid acquisition and low-dose protocols that improve diagnostic accuracy and patient comfort. AI plays a crucial role throughout the PET imaging workflow, from reconstruction to data analysis, facilitating enhanced reporting and exploration of systemic interactions in clinical and research settings. This synergistic approach optimizes TB-PET functionality and promises to revolutionize patient outcomes by streamlining processes and pioneering new applications in medical imaging. Collaborative efforts and shared resources will be essential to fully realize the potential of this AI-TB-PET integration [4, 6].

## 4 Generative Models for PET Image Synthesis

Generative models have significantly advanced the synthesis of Positron Emission Tomography (PET) images, enhancing diagnostic precision and clinical applications. This section explores these models' methodologies and impacts, highlighting how they are reshaping PET imaging and improving patient care.

### 4.1 Applications of Generative Models

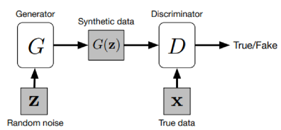
Generative models, especially Generative Adversarial Networks (GANs) and diffusion models, are pivotal in PET image synthesis, enhancing diagnostic accuracy and clinical utility. GANs, like M-GAN, generate high-quality synthetic images by capturing both anatomical and semantic details, crucial for machine learning training in clinical settings focused on reducing radiation exposure and scan times [21, 48]. GANDALF exemplifies GANs' ability to produce realistic datasets, improving Alzheimer's disease classification [49]. Similarly, RadioGAN addresses data scarcity by generating realistic Maximum Intensity Projection (MIP) PET images, expanding PET imaging's applicability and streamlining diagnostics [24].

Diffusion models, such as PET-DDS, excel in reconstructing low-count PET data to closely match full-count reconstructions, achieving lower variance and superior image quality [46]. The stability and reliability of these models during training, as demonstrated by ProAGAN, facilitate the generation of synthetic images that closely mimic real ones, enhancing stochastic object model reliability [50]. Integrating generative models with hybrid methods, like the proposed PET/CT reconstruction framework, improves diagnostic accuracy by effectively merging PET and CT images [51]. This integration highlights the importance of combining data-driven insights with physics-based constraints

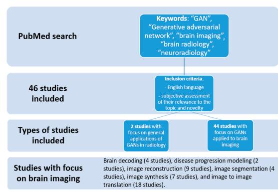
[52]. Wang et al. further emphasize generative models' role in enhancing diagnostic accuracy through improved image quality, providing a proof of concept for their method [53].

Innovative techniques like paired diffusion generation enable the simultaneous generation of related images and annotations, enriching AI models' training data [54]. Observer studies validate the realism of synthetic oncological PET images, confirming their applicability in AI training [55].

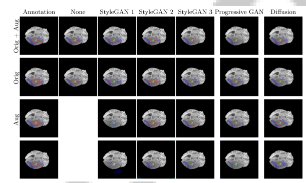
These advancements underscore the transformative potential of generative models in medical imaging, significantly improving diagnostic capabilities and patient outcomes through enhanced image quality and synthesis. By leveraging GANs and diffusion models, medical imaging is progressing notably, enhancing patient care aspects such as data augmentation, image reconstruction, segmentation, and cross-modality synthesis. These technologies address challenges like labeled dataset scarcity and improve diagnostic accuracy. Continued research and application of these models promise to further revolutionize medical imaging, leading to better patient outcomes and more efficient clinical workflows [56, 34, 57, 58, 41].




(a) Generative Adversarial Network (GAN)[22]




(b) Study on the Application of Generative Adversarial Networks (GANs) in Brain Imaging[41]




(c) Comparison of Different Image Restoration Techniques on Brain MR Images[59]

Figure 3: Examples of Applications of Generative Models

As shown in Figure 3, generative models, particularly in PET image synthesis, are transformative in medical imaging. The first example illustrates a GAN's architecture, highlighting its generator-discriminator interplay that produces realistic images vital for diagnostics. The second example analyzes GANs' application in brain imaging, emphasizing a thorough literature review process via PubMed to consolidate understanding of GANs' medical effectiveness. Lastly, the comparison of image restoration techniques on brain MR images demonstrates generative models' versatility, such as StyleGAN and diffusion models, in enhancing image quality. This comparison not only showcases advancements in image restoration but also emphasizes these models' potential to revolutionize medical imaging data processing and interpretation, underscoring their significant impact on improving PET imaging accuracy and efficacy [22, 41, 59].

# 5 Deterministic Methods and Their Integration with AI

The integration of deterministic methods with artificial intelligence (AI) in medical imaging marks a significant advance, enhancing diagnostic practices by addressing complexities in clinical data interpretation. This synergy not only improves imaging capabilities but also optimizes diagnostic accuracy and workflow efficiency in clinical settings.

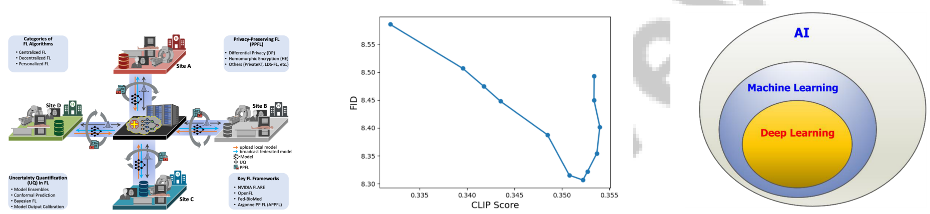
## 5.1 Applications of Deterministic and AI Integration in Clinical Settings

The fusion of deterministic methods with AI has significantly advanced Positron Emission Tomography (PET) imaging, enhancing diagnostic accuracy and efficiency. Denoising Diffusion Probabilistic Models (DPM) exemplify this integration by improving PET image reconstruction, highlighting the synergy between deterministic approaches and AI for optimized image quality and diagnostics [29]. Generative Adversarial Networks (GANs) are pivotal in data augmentation, enhancing tumor detection sensitivity in brain magnetic resonance (MR) images and improving clinical outcomes. The i-SIS method demonstrates the successful integration of deterministic and AI techniques in PET imaging, enhancing anatomical detail and reducing noise, thus supporting clinical applications by overcoming limitations like high noise and low resolution critical for accurate PET assessments [3, 6].

Research highlights the importance of addressing challenges such as dependency on high-quality training datasets and model generalizability across modalities. AI-driven confidence scores in PET imaging improve image accuracy and reliability, facilitating rapid, low-dose protocols that enhance patient comfort and diagnostic capabilities, thereby optimizing the synergy between AI and advanced imaging technologies in nuclear medicine [3, 5, 6]. Cross-modality synthesis from CT to PET images eliminates manual labeling, streamlining detection systems and showcasing AI's practical benefits in clinical workflows.

The implementation of 3D conditional Generative Adversarial Networks (3D-cGAN) for PET image synthesis offers a cost-effective, non-invasive method enhancing generative models' clinical utility. This approach generates realistic PET images conditioned on tumor masks, ensuring precise control over tumor geometry and location, while segmentation-guided techniques preserve critical features, addressing radioactive exposure concerns in full-dose imaging [60, 23]. Active learning frameworks with transfer learning reduce annotation costs while maintaining performance, and GAN augmentation enhances segmentation, demonstrating successful clinical integrations.

These advancements underscore the transformative impact of integrating deterministic methods with AI, improving diagnostic accuracy, patient outcomes, and imaging efficiency. The Total-Body PET (TB-PET) system enhances diagnostics through improved sensitivity, enabling rapid, low-dose imaging that elevates patient comfort and diagnostic accuracy. AI optimizes the entire PET imaging workflow, streamlining processes and pioneering new applications, addressing challenges like complexity and standardized protocols, revolutionizing patient care and advancing clinical practice in nuclear medicine [7, 6, 4, 10, 3].




(a) Privacy-Preserving Federated Learning (PPFL) in Healthcare: A Comprehensive Overview[61]

(b) The graph shows the relationship between the CLIP score and the FID score for a dataset.[62]

(c) Deep Learning is a subset of Machine Learning, which is a part of Artificial Intelligence (AI).[63]

Figure 4: Examples of Applications of Deterministic and AI Integration in Clinical Settings

As shown in Figure 4, the integration of deterministic methods with AI in clinical settings is illustrated through various applications. The first image highlights Privacy-Preserving Federated Learning (PPFL) in healthcare, showcasing federated learning algorithms employed with privacy-preserving techniques to securely manage data across sites. The second figure presents a graph demonstrating the relationship between CLIP and FID scores, offering insights into performance metrics for AI models in medical imaging. Lastly, the third image uses a Venn diagram to clarify the hierarchical relationship between AI, machine learning, and deep learning, illustrating deep learning's contribution to AI. These examples underscore the potential of combining deterministic methods with AI to advance clinical applications, ensuring efficacy and privacy in healthcare innovations [61, 62, 63].

### 5.2 Hybrid and Multi-modal Approaches

The integration of hybrid and multi-modal approaches in Positron Emission Tomography (PET) imaging has significantly advanced the field by combining functional and anatomical data from various modalities, such as PET-CT and PET-MRI, to improve diagnostic accuracy and image quality. This evolution includes simultaneous functional PET/MR techniques for concurrent brain network monitoring and the innovative Total-Body PET (TB-PET) system, enhancing sensitivity and reducing imaging time. AI integration in these workflows transforms data analysis and acquisition, facilitating rapid imaging and enabling a deeper understanding of physiological and pathological conditions, maximizing multi-modal imaging's potential in clinical and research settings [6, 64, 65, 66].

One notable advancement is the integration of PET with Magnetic Resonance Imaging (MRI), providing both functional and anatomical information, enhancing diagnostic precision. This synergy improves attenuation correction and anatomical localization, crucial for accurate diagnosis and treatment planning [16]. AI-driven methods, like deep learning networks for simultaneous PET and MRI reconstruction, optimize image quality and diagnostic utility [20].

Hybrid approaches extend to PET with Computed Tomography (CT), forming PET/CT systems offering functional and structural insights. This combination enhances lesion detection accuracy and characterization, aiding precise anatomical localization essential for treatment planning [27]. AI techniques, such as convolutional neural networks (CNNs), in PET/CT systems enhance image reconstruction and noise reduction, contributing to superior image clarity and diagnostic performance [17].

The integration of hybrid and multi-modal approaches is exemplified by frameworks utilizing data-driven insights and physics-based constraints. These frameworks, employing multi-hypothesis deep learning models, enhance PET image reconstruction's robustness by incorporating diverse data sources [20]. Multi-modal data fusion techniques, integrating information from PET, MRI, and CT, further illustrate hybrid approaches' potential to improve diagnostic accuracy and patient outcomes.

The ongoing advancement of hybrid and multi-modal approaches in PET imaging is revolutionizing diagnostics by enabling simultaneous acquisition of functional and anatomical data, enhancing disease characterization accuracy, and improving patient comfort through rapid, low-dose protocols. Innovations like PET-MRI and Total-Body PET expand imaging systems' capabilities, facilitating a deeper understanding of complex physiological processes and disease mechanisms, supported by AI's transformative role in optimizing imaging workflows and data analysis [6, 64, 65, 66]. By combining data from multiple modalities and integrating advanced AI techniques, these approaches significantly enhance image quality, diagnostic precision, and clinical utility, ultimately improving patient care and treatment outcomes.

## 6 Challenges and Future Directions

The integration of artificial intelligence (AI) into Positron Emission Tomography (PET) imaging offers significant advancements but also presents multifaceted challenges. This section explores the hurdles and innovations in AI-based PET reconstruction, focusing on the complexities of embedding AI technologies into clinical workflows and innovative strategies to enhance image quality. As illustrated in Figure 5, the hierarchical structure of challenges and future directions in AI-based PET imaging is categorized into five main areas: AI-based PET reconstruction, data availability and quality, computational costs and efficiency, model generalization and robustness, and ethical and regulatory considerations. Each category is further divided into specific challenges and innovative approaches or future directions aimed at addressing these challenges. This visual representation not only highlights the intricacies involved in the integration of AI into PET imaging but also serves as a roadmap for future research and development in this evolving field.

### 6.1 Challenges and Innovations in AI-based PET Reconstruction

The incorporation of AI in PET reconstruction has led to advancements but also poses challenges that must be addressed for optimal clinical efficacy. A primary issue is the degradation of image quality due to increased statistical noise in low-count PET imaging, impacting the accuracy of reconstructed time activity curves (TACs) and diagnostic precision [18]. High noise levels complicate the imaging process and compromise PET reconstructions' reliability. Additionally, reliance on single low-dose inputs limits prediction enhancements through supplementary information [14].

The limited availability of large datasets for medical imaging, often constrained by privacy regulations, complicates model training and performance [39]. This challenge is exacerbated by the domain gap between structural MRI and PET modalities, hindering cross-modal data integration for improved reconstruction [12]. Existing segmentation methods struggle with PET scan complexities [32], and the inability to generate patient-specific attenuation maps from MR images further undermines accuracy [16]. Misregistration issues can arise from using non-attenuation corrected PET for automatic registration [19].

Innovative approaches are being developed to tackle these challenges, focusing on enhancing image quality, computational efficiency, and model generalizability. Recent methods aimed at minimizing reconstruction errors have outperformed traditional techniques, significantly improving PET image

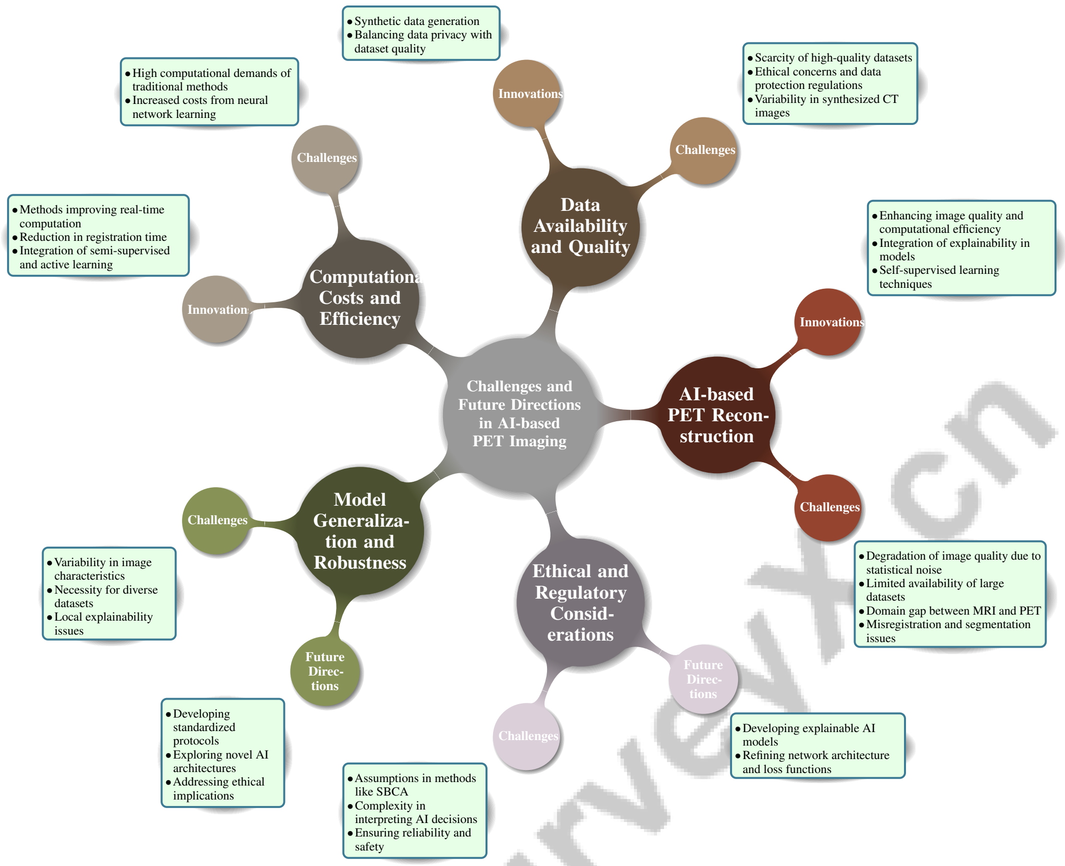



Figure 5: This figure illustrates the hierarchical structure of challenges and future directions in AI-based PET imaging, categorizing them into five main areas: AI-based PET reconstruction, data availability and quality, computational costs and efficiency, model generalization and robustness, and ethical and regulatory considerations. Each category is further divided into specific challenges and innovative approaches or future directions to address these challenges.

quality [1]. Automation of tedious tasks, such as manual segmentation of internal carotid arteries, exemplifies efforts to streamline PET workflows [17].

The integration of explainability in deep learning models is crucial for enhancing clinical acceptance and addressing interpretability and uncertainty issues [2]. Ethical implications, including biases in training data and the complexities of informed consent, remain underexplored [33]. The need for standardized annotation practices and comprehensive evaluation metrics to improve clinical applicability is also emphasized [31].

Innovations in methodologies, such as self-supervised learning techniques, present promising avenues to balance accuracy, speed, and resource consumption in low-dose PET image reconstruction [20]. Addressing both technical and data-related challenges will further enhance patient care and diagnostic capabilities in medical imaging.

### 6.2 Data Availability and Quality

Data availability and quality are critical determinants of AI-based PET imaging effectiveness. The reliance on training data quality and quantity directly influences AI models' generalization ability, a challenge particularly pronounced in medical imaging where high-quality datasets are essential [24]. Current studies face limitations related to data availability, computational demands, and medical imaging tasks' complexity, hindering practical implementation [67].

Ethical concerns and data protection regulations, such as the General Data Protection Regulation (GDPR), exacerbate large, diverse datasets' scarcity, complicating medical images' sharing and



AI-generated, for reference only.

utilization for research [59]. This scarcity is highlighted by the reliance on simulated data for training and real clinical data for validation, underscoring data availability and quality challenges [42].

In synthesizing CT images from MRI data, variability significantly impacts AI model performance and reliability [68]. Models trained on limited datasets may struggle to generalize across diverse clinical settings [3]. Data scarcity often stems from privacy concerns, restricting comprehensive dataset availability. However, synthetic data generation has emerged as a potential solution, augmenting existing datasets while mitigating privacy risks [69]. High-quality PET data are essential for generating accurate ground truth labels in segmentation processes, emphasizing data quality's importance in effective AI model development [70].

To effectively integrate AI into PET imaging, innovative strategies must balance data privacy with high-quality datasets' need. This balance is vital for unlocking AI models' full potential in clinical applications of Total-Body PET (TB-PET), offering enhanced sensitivity and diagnostic capabilities. Addressing industry-specific challenges related to standardization and commercialization, alongside promoting collaborative efforts and open-source initiatives, can streamline AI integration throughout the PET imaging workflow, maximizing technology capabilities and improving patient outcomes [10, 4, 6].

### 6.3 Computational Costs and Efficiency

The computational costs and efficiency of AI models in PET imaging are critical for practical implementation and clinical feasibility. Traditional methods, such as Markov Chain Monte Carlo (MCMC), often demand substantial computational resources and time, limiting clinical applicability [71]. The computational demands of 3D PET image reconstruction methods present significant challenges, particularly with large datasets [72].

Innovative approaches have been proposed to address these computational challenges. The JDAM method improves PET image synthesis efficiency, although its comparative analysis with actual PET scans is limited by data availability [73]. The neural KEM method introduces additional computational costs due to the neural network learning step, potentially increasing overall reconstruction time [74]. Similarly, the deep kernel method requires significant computational resources for training, highlighting inherent challenges in AI models for PET imaging [37].

Efforts to enhance computational efficiency include the LMPDNet method, which improves real-time parallel computation of the projection matrix, addressing computational challenges in AI models [11]. The PET-CM method effectively reduces computational time while maintaining high image quality [75]. Additionally, the STPDnet method enhances noise reduction and interpretability in dynamic PET image reconstruction, contributing to improved computational efficiency [13].

Advancements in computational efficiency are also illustrated by Singh et al., who achieved a significant reduction in registration time from 15 minutes to 95 seconds using their proposed method [19]. The integration of semi-supervised learning and active learning, as discussed by Ji et al., allows models to learn from labeled data while intelligently selecting the most informative unlabeled data for labeling, addressing computational costs and efficiency [76].

Future research should explore hybrid models that combine multiple modalities of data, such as medical images and patient records, to improve diagnostic accuracy and comprehensiveness of explanations [2]. By tackling these computational challenges, AI technologies in PET imaging can be optimized, ultimately enhancing diagnostic workflows and patient outcomes.

### 6.4 Model Generalization and Robustness

The generalization and robustness of AI models are essential for ensuring consistent diagnostic accuracy across diverse clinical scenarios in PET imaging. A significant challenge is the variability in image characteristics, which can hinder model generalization. While some models maintain image clarity and structural details, limitations such as higher absolute error in pseudo-CT (pCT) synthesis raise concerns where pCT accuracy is critical [15]. The need for empirical tuning of penalty parameters and reliance on pre-trained filters from MRI data can further restrict the generalizability of certain methods [1].

The reliance on fully-sampled datasets, which are difficult to obtain, often limits studies' ability to adequately address the preservation of local features in images [39]. This underscores the necessity for larger and more diverse datasets to enhance model training and evaluation, particularly given the variability in lesion characteristics [31]. Methods relying on specific patterns, such as symmetrical patterns in brain images, may not generalize well in certain pathological conditions, emphasizing the need for robust models that can adapt to various clinical presentations [32].

Current research often emphasizes local explainability, which may not sufficiently address global interpretability or the potential for models to make decisions for erroneous reasons [2]. This highlights the importance of developing AI models that are not only accurate but also interpretable and transparent in their decision-making processes. The exploration of non-FDG radiotracers in AI applications remains an area with unanswered questions regarding their optimal integration into clinical practice [25].

The challenges of generalization and robustness are further compounded by the risk of models underperforming if training datasets are not representative of testing conditions, impacting their applicability in diverse clinical scenarios [18]. Future research should focus on developing standardized protocols for AI implementation in clinical practice, exploring novel AI architectures, and addressing the ethical implications of AI in healthcare [4]. By addressing these challenges, future research can improve diagnostic accuracy and patient outcomes, facilitating broader clinical adoption of AI technologies in medical imaging.

### 6.5 Ethical and Regulatory Considerations

Ethical and regulatory considerations are crucial in developing and deploying AI within PET imaging, ensuring that technological advancements translate into safe and effective clinical practices. A key ethical concern involves the assumptions made by methods such as the Symmetry Based Cluster Approach (SBCA), which depend on symmetrical patterns in brain images, necessitating caution to avoid misinterpretations that could compromise patient care [32]. The complexity of AI models often leads to challenges in interpreting decisions, emphasizing the need for explainability to gain trust from medical professionals and comply with regulations like the General Data Protection Regulation (GDPR), which mandates the retraceability of AI decisions [2].

From a regulatory perspective, ensuring the reliability and safety of AI models is paramount, as inaccuracies in AI-driven diagnostic tools could adversely affect patient outcomes. Adhering to established safety and efficacy standards in AI development for PET imaging is essential [20]. Integrating robust methods that combine physics-based and data-driven approaches can enhance these tools' accuracy and reliability, aligning with regulatory requirements to ensure patient safety [20].

The responsible implementation of generative AI in healthcare, including PET imaging, requires addressing significant ethical, legal, and algorithmic challenges. These include ensuring data privacy, managing biases in training datasets, and maintaining transparency in AI decision-making processes [33]. Ethical compliance is further underscored by adherence to the principles of the Declaration of Helsinki, ensuring that AI research in PET imaging maintains high ethical standards [20].

Future research should prioritize developing explainable AI models and explore neuro-symbolic AI approaches to enhance clinical decision-making. Additionally, refining network architecture and loss functions could help balance the accuracy of pseudo-CT (pCT) images and PET reconstruction quality, addressing both ethical and technical challenges [2]. By addressing these ethical and regulatory considerations, the field of AI in PET imaging can advance, ensuring that technological innovations contribute to improved patient care and outcomes.

## 7 Conclusion

The incorporation of AI into PET imaging has significantly transformed the field by advancing image reconstruction and enhancing diagnostic precision. AI techniques, such as the neural KAA method, have substantially improved gCT image quality, showcasing AI's potential to elevate diagnostic outcomes. AI-driven approaches, including the UNN method, have consistently enhanced the denoising of low-count PET images, underscoring AI's pivotal role in improving image quality. Cross-modal synthesis, exemplified by the JPDDM, facilitates the synthesis of PET images from MRI scans with increased stability and accuracy, highlighting the potential for cross-modal applications.

Active learning frameworks further demonstrate AI's transformative impact by reducing annotation costs while enhancing model performance, thereby facilitating quicker and more accurate disease diagnosis.

Innovative techniques, such as the clinically translatable direct Patlak reconstruction, enable high-quality parametric imaging from dynamic PET data, improving motion correction and diagnostic efficiency. Tools like PyTomography reinforce AI's role in advancing PET imaging. Enhanced automated lesion segmentation methods have also improved prediction accuracy and reduced false positives in PET/CT scans, contributing to more reliable diagnostic outcomes. Direct PET image reconstruction methods outperform traditional algorithms, exemplifying the advancements AI brings to image quality and reconstruction speed. Additionally, pseudo-MRI-guided methods enhance diagnostic accuracy and efficiency in PET imaging, highlighting ongoing innovations driven by AI.

Collaboration in standardization and addressing regulatory and clinical adoption challenges is essential for the widespread implementation of AI in PET imaging. As AI continues to evolve, its potential to transform PET imaging through improved diagnostic accuracy and efficiency is evident, promising significant advancements in patient care and clinical outcomes. The proposed PCSA-GAN model exemplifies AI's role in enhancing PET imaging and its potential to boost diagnostic accuracy in clinical settings. The virtual PET estimation method further underscores AI's clinical applications, particularly in tumor detection and treatment evaluation. The BCD-Net significantly improves reconstruction quality in low-count PET scenarios, outperforming traditional methods and demonstrating AI's transformative impact on PET imaging. Moreover, the ICA-net and MCIF-net models enhance the accuracy of carotid artery segmentation and blood input function estimation, validating their clinical relevance.

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