

ARTIFICIAL INTELLIGENCE IN NUCLEAR ONCOLOGY: A REVIEW OF CURRENT EVIDENCE AND TRANSLATIONAL PRIORITIES

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Abstract

Artificial intelligence (AI) is fundamentally reshaping the practice of nuclear medicine in oncological diagnosis. This review systematically evaluates the technological foundations, clinical applications, diagnostic performance, and barriers to clinical translation of AI in nuclear medicine for cancer diagnosis. A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science databases for studies published between 2020 and 2025. Studies were categorized by AI methodology (radiomics, deep learning, large language models) and clinical application (diagnostic classification, treatment response prediction, prognosis, image enhancement, dosimetry). Current evidence demonstrates that AI-driven radiomics models achieve significant performance improvements in diagnostic classification across multiple tumor types, while deep learning assistance enhances clinician diagnostic sensitivity and accuracy. In radiopharmaceutical therapy, AI-supported individualized dosimetry strategies show potential for simplified imaging protocols. Large language model applications in nuclear medicine expanded from 41 tasks in 2023 to 434 tasks in 2025. However, insufficient data standardization, lack of external validation, limited model interpretability, and unclear regulatory pathways remain significant barriers to clinical translation. Future research should focus on prospective multicenter validation, standardized imaging protocol development, and explainable AI frameworks.

1. INTRODUCTION

Nuclear medicine occupies a unique position in oncological imaging through its capacity to visualize molecular processes rather than mere anatomical structures. Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) enable non-invasive assessment of tumor metabolism, receptor expression, and molecular pathway activity, playing an irreplaceable role in cancer diagnosis, staging, and treatment response evaluation [1]. The emergence of novel tracers targeting prostate-

specific membrane antigen (PSMA), fibroblast activation protein (FAP), and amino acid transporters has substantially expanded the oncological applications of nuclear medicine [2]. Concurrently, artificial intelligence (AI)—particularly machine learning (ML) and deep learning (DL)—is fundamentally transforming medical imaging analysis. In nuclear medicine, AI integration has been characterized as a breakthrough development following hybrid imaging and novel tracer introduction [3]. AI technologies can automate processing of large-

scale imaging data and extract high-dimensional quantitative features (radiomics) from pixel-level information imperceptible to human observers, thereby supporting diagnostic classification, prognostic stratification, and treatment decision-making [4].

Despite this promise, clinical translation of AI in nuclear oncology faces substantial challenges. Most published models are developed and validated on single-center retrospective data, limiting external generalizability. Heterogeneity in image acquisition protocols, segmentation methods, and feature extraction pipelines impedes cross-institutional reproducibility [5]. Furthermore, regulatory frameworks, reimbursement pathways, and the "black box" nature of deep learning models affect clinician trust and adoption [6].

This review systematically examines the technological foundations, clinical applications, current limitations, and future directions of AI in nuclear medicine for oncological diagnosis, providing an integrated perspective for researchers and clinicians.

2. Technological Foundations of Nuclear Medicine Imaging in Oncology

2.1 Principles of PET and SPECT Molecular Imaging

PET detects positron annihilation photons (511 keV) to reconstruct three-dimensional tracer distributions, while SPECT utilizes single-photon emitting radionuclides for tomographic acquisition. Both modalities provide functional imaging reflecting biochemical processes rather than solely anatomical structure [7].

In oncology, ^{18}F -FDG PET/CT remains the most widely applied metabolic imaging modality, reflecting glucose transport and hexokinase activity [8]. However, FDG specificity is limited by physiological uptake in inflammatory and infectious sites. Novel probes including PSMA-targeted agents for prostate cancer, FAP inhibitors for tumor microenvironment imaging, and amino acid tracers for brain tumors have substantially improved molecular targeting specificity [9].

2.2 Hybrid Imaging and Quantitative Analysis

Clinical adoption of PET/CT and SPECT/CT enables precise anatomical localization of functional uptake, improving lesion detection and staging accuracy [10]. Quantitative parameters including maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) provide objective and reproducible metrics for treatment response assessment [11]. However, conventional quantitative analysis relies on manual or semi-automated lesion delineation, introducing inter-observer variability and limiting extraction of high-dimensional information inherent in imaging data [12].

3. Artificial Intelligence Framework in Nuclear Medicine

3.1 Machine Learning and Deep Learning Methods

AI applications in nuclear medicine span a broad methodological spectrum from traditional machine learning algorithms (support vector machines, random forests, XGBoost) to deep learning architectures (convolutional neural networks, U-Net, generative adversarial networks) [13]. Traditional ML methods primarily depend on hand-crafted radiomic features, suitable for limited-sample studies [14]. DL models automatically learn hierarchical feature representations from raw images, demonstrating advantages in segmentation, classification, and reconstruction tasks [15].

In PET image reconstruction, DL methods can be categorized into data-driven and model-driven approaches. Data-driven methods directly learn image reconstruction from projection data but require substantial computational memory and training samples; model-driven methods integrate statistical iterative reconstruction methods into deep networks, offering higher training data efficiency and representing a more promising technical pathway [16].

3.2 Radiomics and Radiogenomics

Radiomics extracts high-throughput imaging features—first-order statistics, texture features, shape features, and higher-order wavelet features—

transforming medical images into quantitative data matrices amenable to mining [17]. In nuclear medicine, PET/CT and SPECT/CT radiomics have been applied to predict molecular tumor characteristics and clinical outcomes [18]. For example, radiomics models based on ^{18}F -FDG PET/CT have demonstrated potential for predicting axillary lymph node metastasis burden in breast cancer, potentially aiding preoperative treatment decisions [19].

3.3 Large Language Models and Generative AI

Since the release of ChatGPT in 2022, large language model (LLM) applications in nuclear medicine have expanded rapidly. A 2025 systematic review documented task growth from 41 to 434 between 2023 and 2025, encompassing information processing (159 tasks), data

management (57 tasks), clinical decision support (56 tasks), and medical education (50 tasks) [20]. In nuclear medicine, LLMs have been applied to report generation, patient communication, literature summarization, and clinical note structuring [21]. A study evaluating ChatGPT-4o for extracting PROMISE V2 classification from PSMA PET reports demonstrated accuracy of 85.9%-100% for miN and 89.1%-95.7% for miM staging, but only 57.7% for miT staging in PET/CT reports, significantly lower than the 83.8% achieved in PET/MRI reports. This discrepancy was primarily attributed to ambiguous descriptions of tumor multifocality and extraprostatic extension in free-text reports [22]. However, hallucination—generation of fictitious or erroneous information—poses significant risks to diagnostic accuracy and clinical trust [23].

Table 1. Distribution of Large Language Model Applications in Nuclear Medicine (2023–2025)

Task Category	2023 (n)	2025 (n)	Representative Applications
Information Processing	15	159	Report summarization; literature extraction
Data Management	8	57	Structured reporting; database curation
Clinical Decision Support	6	56	Diagnosis assistance; treatment recommendations
Medical Education	5	50	Training material generation; quiz creation
Patient Communication	4	42	Explanation of findings; preparation instructions
Other	3	70	Administrative tasks; coding
Total	41	434	—

4. Clinical Applications of AI in Oncological Nuclear Medicine Diagnosis

4.1 Diagnostic Classification and Lesion Detection

AI models have demonstrated performance comparable to experts across multiple tumor types in nuclear medicine imaging. In breast cancer, a radiomics nomogram based on ^{18}F -FDG PET/CT was developed to predict axillary lymph node

status after neoadjuvant chemotherapy, integrating primary tumor PET/CT radiomic features with clinicopathological variables [24]. In PSMA PET/CT, the aPROMISE deep learning segmentation and reporting software demonstrated high inter-reader agreement ($\kappa \geq 0.74$) compared with standard image viewers, automatically segmenting 92.1% of consensus

lesions, indicating that AI can serve as a support tool for PSMA PET/CT assessment [25].

4.2 Treatment Response Prediction and Prognostic Assessment

AI demonstrates potential for predicting chemotherapy, immunotherapy, and radiotherapy response. In immunotherapy, PET/PD-L1 expression imaging is emerging as a potential complement to traditional immunohistochemistry, with AI-driven radiomics models potentially enhancing non-invasive prediction of PD-1/PD-L1 expression status [26]. Dynamic imaging (4D PET) provides additional information, such as "intratumoral metabolic heterogeneity factors," which have been used to predict EGFR mutation status in lung adenocarcinoma, offering an imaging surrogate for molecular subtyping [27].

4.3 Image Quality Enhancement and Low-Dose Imaging

AI applications in nuclear medicine image reconstruction and enhancement encompass denoising, attenuation correction, scatter correction, and low-dose/rapid imaging synthesis. Deep learning models have been applied to

directly estimate time-of-flight information, implement triple-coincidence event recovery to improve sensitivity, and improve PET image reconstruction quality through model-driven approaches [28]. These technologies promise reduced patient radiation exposure and shortened acquisition times.

4.4 Dosimetry Optimization in Radiopharmaceutical Therapy

In radiopharmaceutical therapy (RPT), AI is being explored to simplify individualized dosimetry workflows. Conventional dosimetry relies on serial SPECT/CT acquisitions and time-consuming time-activity curve calculations, presenting significant barriers to routine clinical implementation [29]. Conditional generative adversarial network models can predict voxel-level dose distributions in ^{177}Lu -PSMA therapy from pre-treatment ^{68}Ga -PSMA PET, offering proof-of-concept for reduced post-therapy imaging burden [30]. Single time point (STP) dosimetry strategies have also been systematically reviewed as feasible pathways for simplified personalized dosimetry, reducing imaging sessions without significantly compromising accuracy [31].

Table 2. Key Clinical Applications of AI in Nuclear Oncology

Application Domain	AI Methodology	Imaging Modality	Key Outcome	Ref.
Diagnostic classification	Radiomics nomogram	^{18}F -FDG PET/CT	Prediction of axillary lymph node status in breast cancer	[24]
Lesion detection	Deep learning (aPROMISE)	PSMA PET/CT	High inter-reader agreement ($\kappa \geq 0.74$); 92.1% consensus lesions segmented	[25]
Treatment response prediction	Radiomics + ML	^{18}F -FDG PET/CT	Prediction of chemotherapy response in breast cancer	[26]
Prognostic assessment	Radiomics + AI	^{18}F -FDG PET/CT	EGFR mutation prediction in lung adenocarcinoma	[27]

Application Domain	AI Methodology	Imaging Modality	Key Outcome	Ref.
Image enhancement	Deep learning	PET/CT	Improved image quality; reduced radiation dose	[28]
Dosimetry optimization	Conditional GAN	^{68}Ga -PSMA $\rightarrow$ ^{177}Lu -PSMA	Voxel-level dose prediction; reduced post-therapy imaging	[30]
Single time point dosimetry	Systematic review	Various RPT	Reduced imaging sessions without significant accuracy loss	[31]
LLM-based report extraction	ChatGPT-4o	PSMA PET/CT	miN accuracy 85.9–100%; miM 89.1–95.7%; miT 57.7%	[22]

5. Challenges and Limitations

5.1 Data Standardization and External Validation

Heterogeneity in nuclear medicine imaging—including scanner models, acquisition protocols, reconstruction algorithms, and radiopharmaceutical preparation—constitutes a core barrier to cross-institutional AI model generalizability [32]. Most published models are developed and validated on single-center data without prospective multicenter external validation. Radiomic feature reproducibility is affected by segmentation methods, pixel spacing, and gray-level discretization parameters, with incomplete reporting of these parameters in current literature further undermining result replicability [5].

5.2 Interpretability and Clinical Trust

The "black box" nature of deep learning conflicts with clinical decision-making requirements for transparency. Explainable AI (XAI) methods—such as Grad-CAM, LIME, and SHAP—have been applied to nuclear medicine models to visualize voxel-level features attended to by the model. In nuclear medicine, XAI must prioritize stability (against scan noise) and plausibility (ensuring consistency with physical models) to promote clinician trust [5]. However, the practical value of

XAI methods in clinical workflows remains to be prospectively validated [6].

5.3 Regulatory and Implementation Barriers

Clinical adoption of AI tools depends not only on technical performance but also on regulatory approval, reimbursement pathways, and implementation costs. Insufficient model generalizability, data privacy concerns, and ethical dilemmas constitute systemic barriers to AI clinical translation [6]. Furthermore, the complexity of multimodal data integration—requiring fusion of nuclear medicine imaging with electronic health records, laboratory results, and patient-generated data—further increases technical implementation challenges [3].

6. Future Directions

6.1 Multimodal Data Fusion and Digital Twins

Integrating nuclear medicine imaging with clinical, genomic, liquid biopsy, and electronic health record data represents a critical pathway toward precision oncology [33]. The digital twin concept—patient-specific computational models capable of simulating disease trajectories and treatment responses—combined with AI-driven dosimetry prediction holds promise for individualized treatment planning [34].

6.2 Federated Learning and Multicenter Collaboration

Federated learning enables multi-institutional model training without sharing raw patient data, offering a technical solution to the tension between data privacy and sample size limitations [35]. Establishing consensus reference datasets, standardized benchmarking, and coordinated quality control protocols are prerequisites for advancing the field from fragmented research to integrated clinical science [36].

6.3 Prospective Validation and Clinical Integration

Current evidence predominantly derives from retrospective studies with selection bias and data leakage risks [37]. Future efforts require prospective trials in real-world clinical settings to evaluate the substantive impact of AI-assisted diagnosis on patient outcomes (not merely surrogate endpoints such as AUC) [38]. Seamless integration of AI into clinical workflows—including human-computer interface optimization, standardized reporting, and clear accountability frameworks—will be critical determinants of sustainable adoption [39].

7. Conclusion

Artificial intelligence is reshaping the technological landscape of nuclear medicine for oncological diagnosis. From radiomics-driven diagnostic classification and treatment response prediction to DL-enhanced image reconstruction and individualized dosimetry, AI demonstrates substantial potential to improve diagnostic accuracy, optimize workflows, and expand the quantitative dimensions of molecular imaging. However, the retrospective nature of current evidence, data heterogeneity, insufficient model interpretability, and regulatory uncertainty constitute significant gaps between research and routine clinical practice. Future progress will depend on advancing prospective multicenter validation, establishing standardized protocols, and fostering sustained collaboration among clinicians, data scientists, regulators, and patients. The role of AI in nuclear medicine should be

positioned as a decision-support tool that augments rather than replaces clinical expertise.

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