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Seminars in NUCLEAR MEDICINE

The Role of AI in the Evaluation of Neuroendocrine Tumors: Current State of the Art

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Advancements in Artificial Intelligence (AI) are driving a paradigm shift in the field of medical diagnostics, integrating new developments into various aspects of the clinical workflow. Neuroendocrine neoplasms are a diverse and heterogeneous group of tumors that pose significant diagnostic and management challenges due to their variable clinical presentations and biological behavior. Innovative approaches are essential to overcome these challenges and improve the current standard of care. AI-driven applications, particularly in imaging workflows, hold promise for enhancing tumor detection, classification, and grading by leveraging advanced radiomics and deep learning techniques. This article reviews the current and emerging applications of AI computer vision in the care of neuroendocrine neoplasms, focusing on its integration into imaging workflows, diagnostics, prognostic modeling, and therapeutic planning.
Semin Nucl Med 00:1-13

Introduction

Neuroendocrine neoplasms (NENs) are a diverse group of tumors characterized by the expression of neuroendocrine markers. While NENs can theoretically arise from neuroendocrine cells throughout the body, gastroenteropancreatic NENs (GEP-NENs) are without question the most common subset.[1−3] Historically considered a rare disease, improved diagnostic methods and screening practices have led to a significant increase in the reported incidence of NENs, revealing a broader prevalence of these tumors than previously understood.[4] NENs are notable for their prominent expression of different neuroendocrine markers. Somatostatin receptors (SSTRs) are among the most clinically relevant markers, which play a significant role in their clinical management. The expression of SSTRs is a characteristic feature of NENs that enables both diagnostic and therapeutic interventions. SSTR imaging, particularly Positron Emission Tomography/Computed Tomography (PET/CT) with radiotracer-linked peptides specific for SSTR2 (e.g. ^{68}Ga-DOTATATE, ^{68}Ga-DOTATOC), has emerged as a powerful tool for the diagnosis, staging, monitoring, and prognostication of NENs.[5,6] Other functional imaging modalities, such as fluorodeoxyglucose (FDG) PET, can provide complementary diagnostic information to SSTR-based imaging as the increased metabolic activity detected by FDG uptake often correlates with more aggressive tumor behavior.[7−9]

Despite fast advancements in diagnostic technology, NENs remain challenging to diagnose and characterize due to their heterogeneous nature, which complicates classification and prognosis. The variable clinical presentation of NENs compounded by their diverse biological behavior—ranging from well-differentiated, indolent neuroendocrine tumors (NETs) to aggressive neuroendocrine carcinomas (NECs)—poses significant challenges in disease classification and prognosis. Differentiating NETs from NECs is crucial for guiding treatment

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Funding: This study was supported by The Lustgarten Foundation. Felipe Lopez-Ramirez, Mohammad Yasrab, Florent Tixier, Satomi Kawamoto, and Linda C. Chu receive salary support from The Lustgarten Foundation. Elliot K. Fishman reports grant support from the Lustgarten Foundation, Siemens, and is the co-founder of HipGraphics.
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https://doi.org/10.1053/j.semnuclmed.2025.02.003

strategies. The most recent WHO classification highlighted these as distinct disease processes requiring different diagnostic and therapeutic strategies.[10] Distinguishing NETs from NECs remains a significant clinical challenge, which underscores the dual diagnostic hurdle in NEN diagnosis: confirming the presence of the tumor and accurately assessing its biological behavior to guide optimal clinical management. The heterogeneity, complex biological behavior, and diverse imaging patterns of NENs, coupled with their reliance on multimodal (i.e., anatomical and functional imaging) diagnostic approaches for characterization, creates an ideal scenario for the integration of artificial intelligence (AI) applications to enhance precision in detection, classification, and treatment planning. AI-driven tools have the potential to address key clinical challenges posed by the complexity and heterogeneity of NETs, including enhancing diagnostic accuracy, refining prognostic models, personalizing treatment planning, and optimizing therapeutic approaches such as peptide receptor radionuclide therapy (PRRT). This article reviews the current status and future directions for the application of AI in the diagnosis, prognosis, and treatment of NENs. AI has proven capabilities in enhancing the clinical management of NENs from multiple aspects, including analysis of serum biomarkers, pathological specimens and genomic signatures. [11] This review focuses on the impact of AI on diagnostic imaging of NENs, including both anatomical and functional imaging. The review also highlights emerging AI methodologies, their potential integration into clinical workflows, and the opportunities and challenges associated with leveraging AI to improve outcomes in NET management.

Common Tasks in AI—Computer Vision

AI applications in medicine are extensive, addressing challenges in diagnostics, drug discovery, treatment planning, and workflow optimization. Within this context, computer vision, a specialized subfield of AI focused on analyzing pattern associations within images, has become particularly critical for diagnostics and medical imaging. By leveraging advanced algorithms, computer vision enables the extraction of characteristic features and pattern analysis from imaging data.[12] Common computer vision tasks can aid in diagnostics, screening, tumor characterization and prognostication algorithms (Figure 1), and can be described as:

1. Segmentation: Assigning voxel-level labels in the image to delineate and isolate specific objects or areas of interest. AI models can automatically delineate tumors and organ structures from surrounding tissues in different imaging modalities, improving lesion detection, localization and volume estimation. The U-Net, the current gold standard for segmentation tasks, is a deep learning architecture that uses a symmetric encoder-decoder architecture to capture fine details while preserving spatial context.[13] An example training pipeline for an AI segmentation task is shown in Figure 2.
2. Classification: Assigning a global label or category to an entire image, or defined region within the image, based on its features. AI classification models can serve a variety of tasks such as differentiating between different

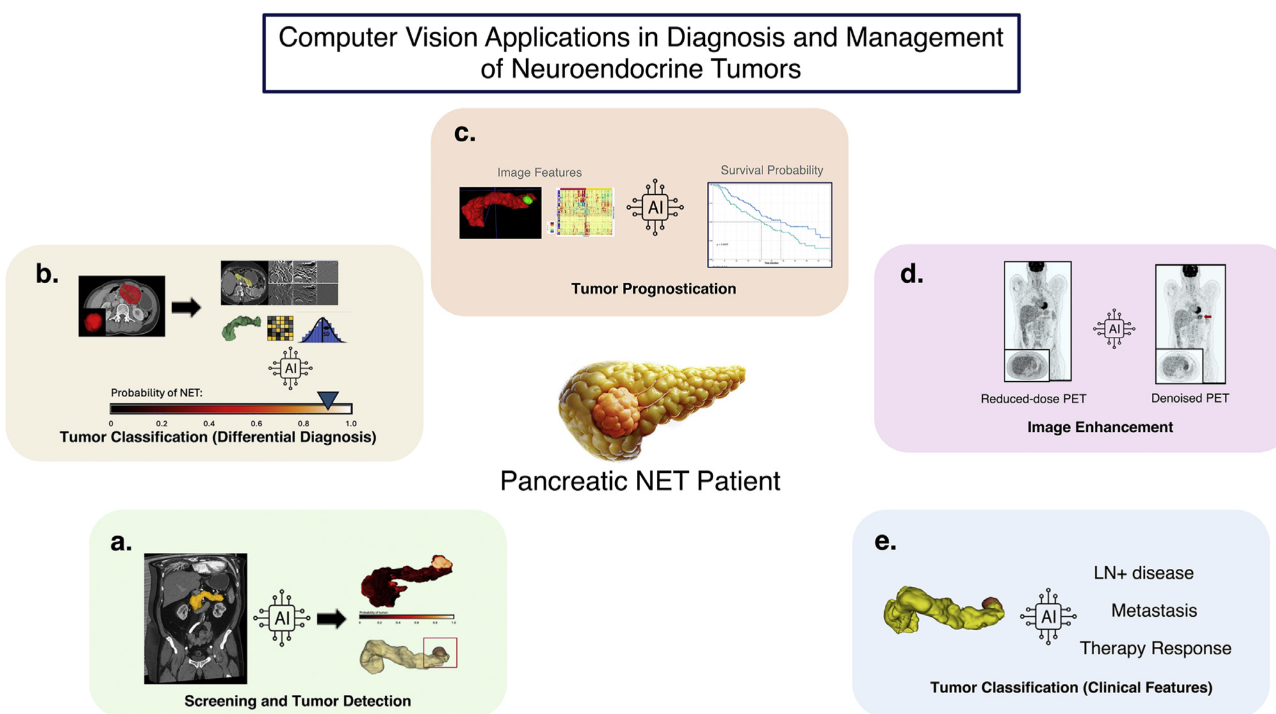

Figure 1 Overview of common AI-driven computer vision applications in the diagnosis and management of neuroendocrine tumors, including (A) screening and tumor detection, (B) differential diagnosis, (C) prognostication, (D) image enhancement, and (E) prediction of relevant clinical features such as lymph node involvement, metastasis, and therapy response.

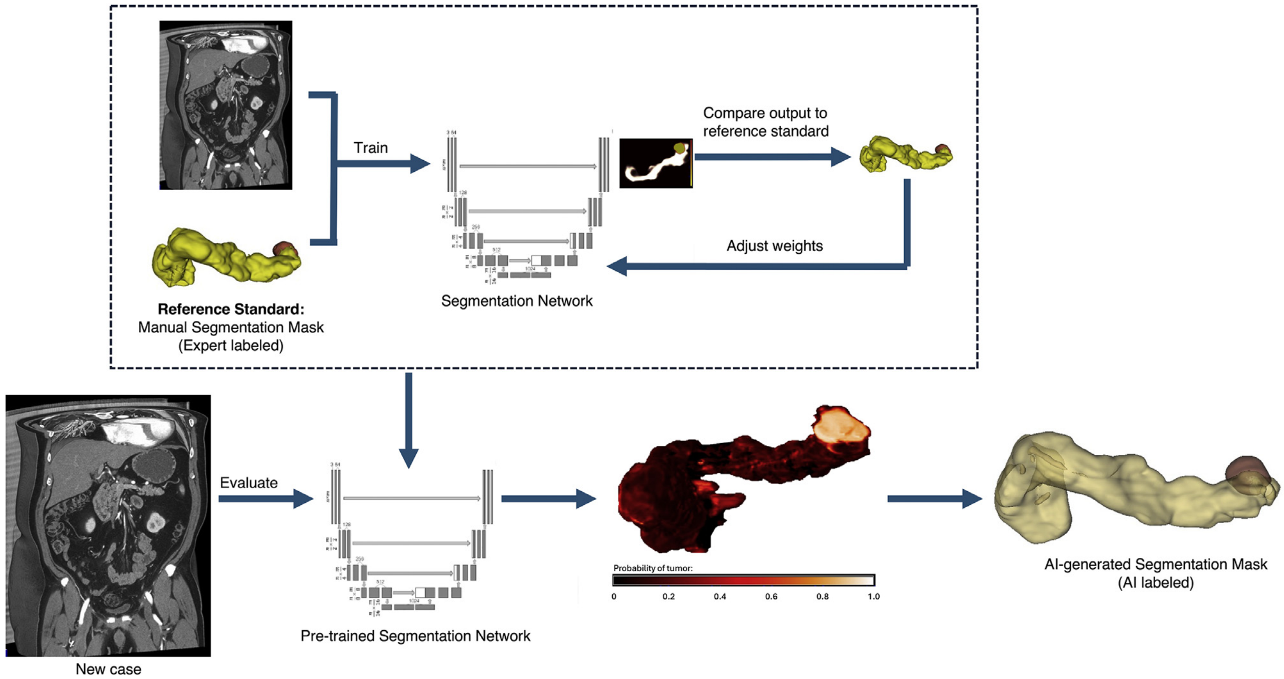

Figure 2 Example workflow for AI-based automatic detection and segmentation of pancreatic structures and neuroendocrine tumors. Initially, a segmentation network is trained using expert-labeled manual segmentation masks as the reference standard. During training, the network's output is compared to the reference, and weights are adjusted accordingly across multiple iterations. Once trained, the network is evaluated on new cases, producing predicted voxel-level segmentation heatmaps and AI-generated segmentation masks for precise pancreatic structure and tumor delineation.

tumor histologic subtypes, or associating imaging features with certain clinicopathological characteristics such as tumor grade or risk of metastases. These models help improve diagnostic accuracy and inform treatment strategies.

3. Prognostic modeling: Integrating imaging and clinical information into a model to predict future outcomes such as progression-free survival or response to therapy. AI models within this task ultimately aid in differentiating higher-risk groups and enable personalized care.
4. Image enhancement: Improving the input image in different aspects such as denoising or augmenting the resolution of low-resolution images to increase their diagnostic value.

Although different approaches exist for AI models to find informative patterns, radiomics models and deep learning architectures are among the most widely used techniques for medical image analysis within the scope of computer vision.[14] Radiomics refers to the high-throughput extraction of quantitative imaging features that characterize tissue phenotypes, such as texture, shape, and intensity, often revealing patterns beyond human perception (Fig. 3).[15,16] Deep learning employs complex neural network architectures, resembling biological neuronal synapses, to identify connections and patterns and extract meaningful features and associations directly from imaging data.[17] Continuous research in machine learning algorithms enables the development of novel configurations that tackle computer vision tasks in innovative ways. For instance, combined segmentation-classification architectures allow simultaneous identification and categorization of regions of interest. Multimodal architectures allow the integration of different inputs, such as anatomical and functional imaging modalities or image data with clinical and genomic data, to provide a comprehensive understanding of disease processes.[18] Recently, the advent of transformers has introduced an additional fast-growing field of research in AI. These transformers models are capable of processing sequential data while preserving context awareness, enabling more efficient predictions and powering advancements such as large language models (LLMs).[19] Together, these methods provide a robust framework for leveraging imaging data in different computer vision tasks.

AI in Clinical Workflow Optimization

AI can impact clinical workflows in diagnostic imaging and nuclear medicine by optimizing imaging processes, reducing radiation exposure, and automating repetitive tasks, aiming to improve clinical efficiency. Previous studies aimed at optimizing diagnostic workflow have showed the potential of machine learning approaches for dual-tracer dynamic imaging, with ^{18}F-FDG and ^{68}Ga-DOTATATE PET/CT in a single

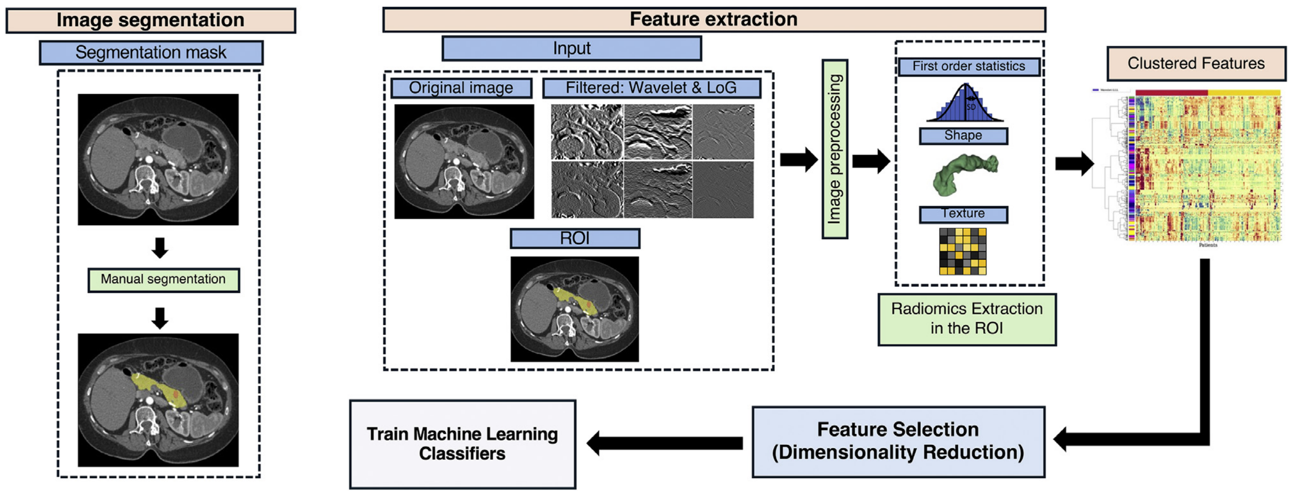

Figure 3 Example workflow for the radiomics features extraction pipeline. The process begins with image segmentation to create region of interest (ROI) masks, followed by feature extraction from original and filtered images using techniques like wavelets and Laplacian of Gaussian. Extracted radiomic features undergo dimensionality reduction and clustering for feature selection to remove redundancy. Final selected features are then used to train machine learning classifiers for different tasks.

session, capable of simultaneously providing information regarding SSTR density and tumor metabolism in NENs.[20] Such AI applications hold significant clinical value, as combined FDG-PET and SSTR-PET provide greater prognostic value in NENs, outperforming traditional pathological grading.[6] Other AI applications address longstanding challenges in functional imaging techniques, such as optimizing image enhancement and improving accuracy in quantitative reporting.

PET/SPECT Image Enhancement

Emerging technologies based on AI have demonstrated potential to transform the image processing pipeline, with special focus on enhancement of functional imaging techniques, such as PET and Single Photon Emission Computed Tomography (SPECT). Due to intrinsic physical and technical constraints, these molecular imaging modalities are limited by high noise levels and reduced spatial resolution, ultimately impacting image quality and their diagnostic value.[21] Traditional denoising techniques often struggle to balance noise reduction with the preservation of critical diagnostic information.[22] AI-based methods, by leveraging deep learning architectures such as convolutional neural networks (CNNs), U-Nets, and generative adversarial networks (GANs), have demonstrated significant advancements in creating high-quality images from low-dose or low-count data.[23−25] Refining post-reconstruction image quality at a computational level through AI enhancement algorithms can potentially reduce the need for hardware upgrades, and improve clinical workflow by shortening scan times and minimizing radiotracer requirements.[26,27] Balaji et al. provided a comprehensive overview of AI-based methods for enhancing PET and SPECT images, showcasing the role of various deep learning architectures in reducing noise and improving spatial resolution. Image denoising models have already shown capabilities of increasing the signal-to-noise ratio in low-count PET imaging, enabling higher image quality without the increase in radiotracer dose.[28]

Despite these advancements, challenges remain before these methods can be effectively implemented in clinical practice. Most studies artificially generate their training data retrospectively from already existing scans by reducing the sampling or introducing noise. Thus, a major challenge lies in generating optimal training and testing datasets without the need of multiple scans (i.e., full-dose and reduced-dose), as well as ensuring that AI models are generalizable across varying noise distributions. Furthermore, the impact of AI-enhanced imaging on diagnostic accuracy is not yet fully understood. Theoretically, enhancing the signal-to-noise ratio allows for significant reductions in radiotracer dose and scan times, while maintaining diagnostic performance and improving the detection of small lesions otherwise obscured by the noise. However, conflicting findings have emerged. For instance, Loft et al. evaluated the impact of AI denoising models on the diagnostic accuracy of enhanced low-dose PET imaging. The authors found that although fidelity-based metrics and subjective image quality improved with CNN-based denoising, the human detection rate of NENs decreased when comparing assessment of full-dose vs AI-denoised ^{64}Cu-DOTATATE PET images.[29] These findings underscore the need for more robust studies to clarify the diagnostic impact of AI image enhancement, and address concerns about generalizability of denoising models. Resolving these challenges is critical to ensuring the safe and effective clinical adoption of AI-powered image enhancement technologies.

Reporting Aided by Large Language Models

LLMs are increasingly being used to optimize diagnostic imaging workflows and radiology reports, transforming the way medical imaging professionals interact with data and perform their tasks. Key applications and developments have emerged such as report structuring and summarization, automation of administrative tasks, as well as error detection and classification in imaging reports.[30,31] Efforts to integrate LLMs with large scale PET imaging databases are underway, with the promise to enhance reporting by generating contextually relevant interpretations, improved decision-making and educational opportunities.[32] By streamlining imaging workflow and improving access to critical patient data, LLMs open new opportunities for efficiency, collaboration, and innovation across the fields of radiology and nuclear medicine.

AI Screening and Diagnosis of NENs

The application of AI in the screening and diagnosis of NENs encompasses two distinct but complementary clinical goals. One approach focuses on the use of AI as an automated screener or "second reader" to enhance early detection by identifying subtle imaging abnormalities that might otherwise be missed. In this type of application, the human reader is unaware of the tumor presence; hence these algorithms are generally designed to prioritize sensitivity, aiming to flag potential abnormalities for further human evaluation. Although very few studies have focused on developing detection algorithms specifically for NENs,[33−35] broader abnormality detection algorithms in different organs can serve as potential screening tools for NENs.[36−39] Cao et al.[36] developed one of the largest pancreatic lesion detection algorithms in noncontrast CT published to date. While their work demonstrated impressive results in overall pancreatic lesion detection in a large external validation cohort, the absence of contrast enhancement and the limited representation of NENs in the training dataset likely contributed to lower accuracy for these tumors. Integrating multimodal imaging techniques may be necessary in these larger models to achieve reliable performance in detecting these more inconspicuous lesions.

Alternatively, in scenarios where a tumor has already been identified, AI can be used to detect imaging patterns associated with different tumor subtypes and help the diagnostician differentiate between NENs and other potential clinical entities. In this context, the reader is aware of the tumor and goes to AI to assist in selecting the most likely option amongst the differential diagnoses. However, a significant barrier to clinical implementation remains the labor-intensive process of manual segmentation required to define regions of interest (ROIs) for feature characterization. Advances in deep learning-based automated segmentation have partially addressed this challenge,[33,40] offering a more efficient and scalable clinical integration.

AI-based segmentation networks can serve multiple purposes during the diagnostic process by automating ROI delineation for feature extraction and estimation of tumor burden in both primary and metastatic contexts. Among recently published studies, the U-Net architecture continues to be the main approach used for this task.[41−43] Approaches such as Carlsen et al.[43] have used ^{64}Cu-DOTATATE PET/CT image information for automated segmentation of NENs, demonstrating a potential reduction in segmentation time from this multimodal combination. An overview of recent published studies on NEN screening, tumor segmentation and differential diagnosis classification is presented in Table 1.

In the context of NEN management, radiomics and deep learning approaches already enable the precise extraction of biomarkers in NEN imaging, yet significant challenges persist in integrating these techniques into clinical workflows. A systematic review by Staal et al.[44] revealed the limited number of studies on GEP-NENs, with most focusing on pancreatic NETs (PNETs) and only a few addressing other regions, such as rectal or gastrointestinal NETs. These studies predominantly utilized CT or MRI for feature extraction, with minimal use of PET/CT imaging techniques with ^{68}Ga-DOTA-peptides or ^{18}F-FDG. The small sample sizes presented (median 61, range 11−157) and low radiomics quality scores (RQS) further hinder the development of robust, clinically relevant models.

AI in Characterization of NENs

In the context of a known NEN, AI models are commonly evaluated in clinical settings to characterize the tumor and predict clinicopathological characteristics that are relevant for determining prognosis. Perhaps due to the high relevance of tumor grade in NENs, along with the high morbidity associated with pancreatic surgery, the most common tumor characterization task among published studies is the prediction of tumor grade in PNETs.[45] Despite the high clinical relevance of differentiating NETs from NECs, with previous exploratory analyses suggesting that imaging features could potentially distinguish between these tumor types,[46] very few studies have explored this task.[47] Most efforts have instead concentrated on differentiating between grades of NETs,[45] likely due to limitations in sample size and the underrepresentation of NECs in institutional databases. An overview of recent published studies around NEN characterization is presented in Table 2.

Although the definitive surgical pathology remains as the gold standard for tumor grading of NENs, some studies have shown promising results towards leveraging radiomics and deep learning models to aid in the grading of NENs and potentially decrease the burden of unnecessary surgical procedures. Nonetheless, the high variability in PNET presentation makes this a daunting task. A systematic review performed by Yan et al.[45] showed a moderate predictive value of machine learning models in predicting PNET grade, with a pooled AUC of 0.89. Although these results are encouraging, the included studies showed high heterogeneity and almost half of the included studies lacked an independent validation group. Most published studies have focused on analyzing features such as texture, intensity, and volumetric patterns from anatomical imaging modalities like CT and MRI to differentiate between low-grade and high-grade NETs (Table 2). Functional imaging has been less commonly

Table 1 Representative Sample of Peer-Reviewed Studies for AI-Aided Screening and Diagnosis of Neuroendocrine Neoplasms

Study	Region (NEN Subtype)	Imaging Modality	Task	Training/Validation Cohort	Independent Testing Cohort	Approach (ML Model)	Summary Metrics*	CLAIM†
Diagnostic: Screening/ Tumor Detection Algorithms								
Lopez-Ramirez et al.[33]	Pancreas (PNET)	CE-CT	Detection: Small PNET (<2 cm) vs normal pancreas	N = 176	N = 94	Radiomics (LightGBM)	AUC: 0.87 (95% CI: 0.79-0.94), Acc: 0.83 SENS: 0.90, SPEC: 0.76	35/41
Shin et al.[34]	Small Bowel	CE-CT	Detection: Overall lesion detection	N = 24 (5-fold CV)	N = 9 + N = 22 negative controls	Deep Learning (nnDetection)	Patient level detection: AUC: 0.86 (95% CI: 0.81-0.91), SENS: 0.78, SPEC: 0.82	29/42
Cao et al.[36]	Pancreas (PNET)	NC-CT	Detection: Overall pancreatic lesion detection	N = 3,208	External test cohort for lesion subtypes: (N=3,699; N=160 PNET)	Deep Learning (nnUNet)	Overall pancreatic lesion detection: AUC: 0.984 (95% CI: 0.980-0.987 PNET detection rate: 0.56	40/42
Wehrend et al.[59]	GEP-NET Liver METS	68Ga- DOTATATE PET/CT	Detection: Overall liver lesion detection	N = 75 + N = 25 (Validation)	N = 25	Deep Learning (2D U-Net)	AUC: 0.73, SEN: 0.69, PPV: 0.90	30/42
Diagnostic: Tumor Differentiation/Classification								
Shen et al.[60]	Pancreas (PNET)	MP-MRI	Classification: small (<2 cm) PDAC vs PNET	N = 146	N = 51	Radiomics + clinical features (LASSO-logistic regression)	AUC: 0.94 (95% CI: 0.875-0.999), SENS: 0.852, SPEC: 0.950	34/42
Liu et al.[61]	Lung (LNEN)	NC- CT	Classification: LNEN vs LADC	N = 316 (10-fold CV)	N = 129	Radiological signs + radiomics (SVM)	AUC: 0.807 (95% CI: 0.720-0.889), SENS: 0.84, SPEC 0.60	33/43
Shi et al.[62]	Pancreas (PNET)	MRI (DWI)	Classification: PDAC vs SPEN vs PNET	N = 92 + N = 46 (Validation)	N= 93	Deep learning (CNN)	PDAC vs non-PDAC: AUC:0.817 (95%CI: 0.739-0.896), SENS: 0.91, SPEC: 0.70	32/42
Cao et al.[63]	PGL	NC + CE- CT	Classification: Retroperitoneal PGL vs schwannoma	N = 63 + N = 25 (Validation	N = 24	Radiomics + clinical features (logistic multiple regression)	AUC: 0.871 (95% CI: 0.710-1.00), Acc: 0.92, SENS: 0.92, SPEC: 0.82	29/42
Zhang et al.[64]	Pancreas (PNET)	CE- CT	Classification: PDAC vs PNET	N=238	25% of the cohort	Radiomics (RF)	AUC: 0.93, SENS: 0.74, SPEC: 0.93	24/41
Chu et al.[65]	Pancreas (cystic PNET)	CE- CT	Classification Pancreatic cyst differential	N= 214 (4-fold CV)	N/A	Radiomics (RF)	Overall cyst: AUC:0.94 Cystic PNET: AUC: 0.90	28/40
Han et al.[66]	Pancreas (PNET)	CE- CT	Classification: Cystadenoma vs PNET	N = 120	20% of the cohort	Radiomics (RF)	AUC: 0.99, SENS: 0.98, SPEC: 0.99	25/41
Shi et al.[67]	Pancreas (PNET)	MP-MRI	Classification: SPEN vs PNET	N = 44	N=22	Radiomics+ clinical features (LASSO-Logistic Regression)	AUC: 0.86 (95% CI: 0.69-1.00), SENS: 0.91, SPEC: 0.82	28/40
Yi et al.[68]	Adrenal (PHEO)	CE- CT	Classification: PHEO vs adrenal adenoma	N = 212	N = 53	Radiomics + clinical features (LASSO- logistic multiple regression)	AUC: 0.967 (95%CI: 0.928-1.000), SENS: 0.999, SPEC: 0.889	28/43
Segmentation: Tumor Burden Calculation								
Haque et al.[42]	PHEO/ PGL (PPGL), GEP-NET	68Ga- DOTATATE PET/CT	Segmentation: METS tumor burden	N = 20 PPGL patients, 70 scans (5-fold CV)	PPGL (N = 18), GEP-NET (N = 9)	Deep Learning (nnU-Net)	Lesion-level DSC: 0.88 (PPGL), 0.60 (GEP-NET). Lesion-level SENS: 0.86 (PPGL), 0.61 (GEP-NET).	31/43
Santilli et al.[69]	Multiple NETs	68Ga-DOTATATE PET/CT	Segmentation: Whole body total tumor	N = 828 scans	N = 87 scans	Deep Learning (nnU-Net)	DSC: 0.64, SENS: 0.66	31/43
Carlsen et al.[43]	GEP-NET, Lung	64Cu-DOTATATE PET/CT	Segmentation: Total tumor	N = 117	N = 41 + N = 10 negative controls	Deep Learning (nnU-Net)	DSC: 0.85, Lesion-level SENS: 0.84	32/43
Fehrenbach et al.[41]	PNET + SB-NEN	Gd-EOB MRI	Segmentation: Liver METS tumor burden	N = 149 patients, 278 scans	N = 33	Deep Learning (nnU-Net)	MCC: 0.86 (IQR: 0.81-0.91)	26/43

Acc, accuracy; AUC, area under the ROC curve; CE, contrast-enhanced; CI, confidence interval; CNN: convolutional neural network; CT, computed tomography; CV, cross-validation; DSC, dice similarity coefficient; DWI, diffusion weighted imaging; GBM, gradient boosting machine; Gd-EOB, gadoxetic acid enhanced; LASSO, least absolute shrinkage and selection operator; LADC, lung adenocarcinoma; LNEN, lung neuroendocrine neoplasm; MCC, Matthew's correlation coefficient; METS, metastases; ML, machine learning; MP-MRI, multiparametric magnetic resonance imaging; N/A, not applicable; NEN, neuroendocrine neoplasm; NC, noncontrast; PGL, paraganglioma; PHEO, pheochromocytoma; PDAC, pancreatic ductal adenocarcinoma; PNET, pancreatic neuroendocrine tumors; RF, random forests; SB-NEN, small bowel NEN; SENS, sensitivity; SPEC, specificity; SPEN, solid pseudopapillary neoplasm.

*Summary metrics from the highest preforming model reported in the evaluation with less risk of bias (i.e., cross-validation results, internal independent test set, OR external validation).

†CLAIM, checklist for artificial intelligence in medical imaging.[70,71] Evaluated a total of 44 items (CLAIM, 2024), reported as number of observed items over the total number of possible categories, excluding N/A items.

Table 2 Representative Sample of Peer-Reviewed Studies for AI-Aided Characterization of Neuroendocrine Neoplasms

Study	Region (NEN subtype)	Imaging modality	Task	Training/Validation cohort	Independent Testing cohort	Approach (ML Model)	Summary Metrics*	CLAIM†
				Tumor Characterization Algorithms				
Tixier et al.[72]	Pancreas (PNET)	CE- CT	Predict tumor grade (G1 vs G2/3)	N = 91	N = 36	Radiomics (SVM)	AUC: 0.79; Acc: 0.78 (95% CI: 0.64-0.89), SENS: 0.92, SPEC: 0.70	33/41
Ye et al.[73]	Pancreas (PNET)	CE- CT	Predict tumor grade (G1 vs G2/3)	N = 122	N=100	Radiomics (RF)	AUC: 0.779 (95% CI: 0.776-0.782), SENS: 0.81, SPEC: 0.75	33/41
Ahmed et al.[74]	Pancreas (PNET)	CE-CT	Predict LN METS	N = 320 (2-fold CV)	N/A	Clinical features + Radiomics (RF)	AUC: 0.80	34/43
Mapelli et al.[75]	Pancreas (PNET)	[68Ga] Ga-DOTANOC PET/CT	Predict LN METS	N = 72 (10-fold CV)	N/A	Radiomics (LDA)	bACC: 0.70, SENS: 0.77, SPEC: 0.61	37/43
Gu et al. [76]	Pancreas (PNET)	CE- CT	Predict LN METS	N = 142 + N = 94 (Internal Validation)	N = 84 (External Validation)	Radiomics + DL features (glmBoost)	AUC: 0.91 (95% CI: 0.85-0.97). SENS: 0.91, SPEC: 0.79	36/43
Park et al.[52]	Pancreas (PNET)	[18F] FDG PET/CT	Predict tumor grade (G1 vs G2/3)	N = 58	N/A	Clinical features + Radiomics (NN)	AUC: 0.86 (95% CI: 0.78-0.95). SENS: 0.72, SPEC: 0.82	33/42
Javed et al.[77]	Pancreas (PNET)	CE- CT	Predict tumor grade (G1 vs G2/3)	N = 201	N = 69	Radiomics + Tumor Size (RF)	AUC: 0.80 (95%CI: 0.70-0.90), SENS: 0.87, SPEC: 0.73	33/42
Mori et al. [78]	Pancreas (PNET)	NC-CT	Predict aggressiveness (i.e., G1 vs G2/3, METS, LN, LVI)	N = 70	N = 31	Clinical features + Radiomics (NN)	G1 vs G2/3: AUC: 0.70	35/42
Liu et al.[79]	Pancreas (PNET)	MultimodaL: CE-CT + MRI	Predict tumor grade (G1 vs G2/3)	N = 82	N = 41	Fusion radiomics model (LDA)	G1 vs G2/3: AUC: 0.85 (95% CI: 0.71-0.94), SENS: 0.84, SPEC: 0.84	29/43
Wang et al[80]	Pancreas (PNET)	CE- CT	Predict tumor grade (G1 vs G2/3)	N = 83	N = 56	Radiomics (SVM)	AUC: 0.84 95% CI: 0.83-0.85), SENS: 0.78, SPEC: 0.84	32/43
Zhang et al.[81]	Pancreas (PNET)	CE- CT	Predict tumor grade	N = 82	25% of the cohort	Radiomics (AdaBoost)	G1 vs G2 AUC: 0.82, SENS: 0.56, SPEC: 0.84 G1 vs G3 AUC: 0.85, SENS: 0.60, SPEC: 0.88	31/42
Bevilacqua et al.[48]	Pancreas (PNET)	[68Ga] Ga-DOTANOC PET/CT	Predict tumor grade (G1 vs G2)	N = 51	N/A	Radiomics	AUC: 0.94, SENS: 0.92, SPEC: 0.85	36/43
Luo et al. [82]	Pancreas (PNET)	CE- CT	Predict tumor grade (G1/2 vs G3)	N = 93	N = 19	Deep Learning: CNN	AUC: 0.82, SENS: 0.88, SPEC: 0.85	32/41
Bian et al.[83]	Pancreas (PNET)	MRI	Predict tumor grade (G1 vs G2/3)	N = 97	N = 42	Radiomics (LDA)	AUC: 0.736 (95% CI: 0.548-0.874)	35/43
Zhao et al.[84]	Pancreas (PNET)	CE-CT	Predict tumor grade (G1 vs G2)	N = 59	N = 40	Radiomics (SVM)	AUC: 0.88 (95%CI: 0.70-0.96), SENS: 0.96, SPEC: 0.84.	32/42

Acc, accuracy; AUC, area under the ROC curve; CE, contrast-enhanced; CT, computed tomography; CV, cross-validation; DSC, dice similarity coefficient; G, grade; LDA, latent Dirichlet allocation; LN, lymph node; ML, machine learning; METS, metastases; MRI, magnetic resonance imaging; N/A, not applicable; NC, noncontrast; NEC, neuroendocrine carcinoma; NET, neuroendocrine tumor; PDAC, pancreatic ductal adenocarcinoma; PNET, pancreatic neuroendocrine tumors; RF, random forests; SENS, sensitivity; SPEC, specificity; SVM, support vector machines.

*Summary metrics from the highest preforming model reported in the least biased cohort evaluated (i.e., cross-validation results, independent test set, external validation).

†CLAIM: Checklist for Artificial Intelligence in Medical Imaging.[70,71] Evaluated a total of 44 items (CLAIM 2024), reported as number of observed items over the total number of possible categories, excluding N/A items.

explored for this task. Bevilacqua et al. evaluated the ability of radiomics models to predict PNET tumor grade using ^{68}Ga-DOTANOC PET/CT, demonstrating the potential of AI to extract imaging biomarkers indicative of tumor grade.[48] These findings suggest that combining advanced imaging techniques with AI could play a pivotal role in noninvasively characterizing NENs. However, further validation studies, with more standardized protocols that overcome the high variability are still needed before these AI applications can migrate into clinical deployment.

AI in Prognostication and Predictive Analytics of NENs

Risk Stratification Models

AI has shown significant results enhanced risk stratification in NENs by analyzing complex datasets to predict patient outcomes more accurately. Most published studies leverage clinical and genomic data to train predictive models to define high-risk patients and predict poor oncological outcomes.[49] Although evidence of AI computer vision models is still limited, some studies are already exploring the role of textural features extracted from functional imaging.[50,51] Park et al.[52] developed machine learning models using ^{18}F-FDG PET/CT-based radiomics to predict tumor grade and risk of recurrence in patients with PNETs. Other studies have demonstrated encouraging preliminary results in predicting PPRT response from features in pre-treatment PET and SPECT images.[53,54] The integration of functional imaging provides valuable insights into tumor biology. Despite being limited by sample size and the absence of external validation, these models demonstrated encouraging potential in using AI to leverage molecular imaging features as noninvasive tools to stratify patient risk and improve clinical decision-making. An overview of recent published studies around this task is presented in Table 3.

AI in Precision Medicine for NENs—Theranostics

Fast technological advancements in PRRT have continuously expanded the utilization of SSTR-targeted imaging and therapy for NETs, enhancing the detection and characterization of NETs and enabling personalized treatment strategies. A key challenge in PRRT is accurately calculating the radiation dose absorbed by tissues at a voxel-level spatial resolution. Voxel-level dosimetry enables a precise mapping of the absorbed dose in both tumor targets and surrounding healthy tissues, allowing personalized treatment planning.[55] However, personalized manual dosimetry estimation is labor intensive and time consuming. Dewaraja et al. proposed an automated pipeline that integrates AI-based segmentation, image registration, dosimetry calculations, and curve fitting. Their approach demonstrated comparable accuracy to traditional manual dosimetry methods, while significantly improving efficiency and streamlining the process.[56]

AI implementation in this emerging therapeutic field has focused mainly on outcome prediction, aiming to enhance treatment planning and prognostication. Akhavanallaf et al. showed a preliminary model to predict tumor absorbed dose in metastatic NET patients undergoing ^{177}Lu-DOTATATE therapy using pretherapy ^{68}Ga-DOTATATE PET imaging and clinicopathological biomarkers. These results show a potential application of AI in predicting PRRT therapeutic response.[57] Utilizing a combination of radiomic features derived from CT imaging data, and dosiomic features extracted from the dose map, Plachouris et al.[58] developed a model capable of predicting absorbed doses to critical organs and tumor lesions. Although limited by a small sample size and lack of an independent test set, these preliminary results in dose-response modeling emphasize the potential for enhanced precision in ^{177}Lu-DOTATATE therapy, enabling clinicians to tailor treatments based on individualized predictions. These advancements underscore the transformative potential of AI in prognostication and predictive analytics, paving the way for more personalized and effective management of NENs, enhancing treatment efficacy and minimizing adverse effects.

Challenges and Future Directions

Despite encouraging results, many barriers remain before AI models can be widely applied to support the clinical management of NENs. While most challenges are common across AI applications in medicine, the relative rarity of NENs and high heterogeneity in tumor biology and disease presentation amplify these difficulties. A major challenge with AI lies in the generalization of algorithms beyond the training cohort, often resulting in significant performance reductions for underrepresented groups. Most current NENs AI studies have sample sizes too small to develop robust, generalizable models, emphasizing the urgent need for collaborative efforts to create publicly available annotated imaging datasets in NENs. These datasets would enable large-scale training of radiomics and deep learning models, which are critical for improving AI performance and generalizability. Additionally, studies must prioritize demonstrating the clinical value of AI-predictions through standardized prospective studies compared with current diagnostic gold standards, a key step toward ensuring clinical relevance.

The complexity of NEN diagnosis lays the foundation for the integration of advanced AI tools, which possess a powerful ability to identify hidden patterns in imaging data and integrate multimodal information. Even with the fast technological advancements in diagnostic technology, NENs remain challenging to diagnose and characterize due to their heterogeneous nature, which can complicate classification and prognosis. Despite the development of highly specific radiotracers, false negatives can still occur depending on tumor biology. Moreover, the positive predictive value of functional imaging might be confounded by significant levels of physiologic uptake of radiotracers.[6] Everyday AI architectures become more sophisticated, allowing for a more

Table 3 Representative Sample of Peer-Reviewed Studies for AI-Aided Prognostication and Prediction of Therapeutic Response of Neuroendocrine Neoplasms

Study	Region (NEN subtype)	Imaging modality	Task	Training cohort	Independent Testing cohort	ML Approach (Model)	Summary Metrics*	CLAIM†
				Tumor Prognostication Algorithms				
Polici et al.[85]	GEP-NET	CE- CT	Predict response to SSA	N = 55	N/A	Radiomics + Ki-67 (Multivariable logistic regression)	AUC: 0.81, Acc: 0.74	24/39
Heo et al. [86]	Pancreas (PNET)	CE- CT	Predict RFS	N = 441	N = 159	Clinical features + Radiomics (LASSO + Cox regression)	C-index for RFS: 0.734 (95% CI: 0.67-0.79)	36/43
Behmanesh et al.[87]	NET METS	CE- CT	Predict response to PRRT	N = 34	N/A	Radiomics (RF)	Acc: 0.74, SENS: 0.65, SPEC: 0.91	33/43
Homps et al.[88]	Pancreas (PNET)	CE- CT	Predict RFS	N = 37	N/A	Radiomics (Linear fitting model)	High risk: RFS of 36 months (IQR: 15-74 months), Low-risk RFS of 84 months (IQR: 33-108, *P*-value = 0.013)	32/40
Yang et al.[89]	GNEN	CE- CT	Predict OS	N = 128	N = 54	Clinical features + Radiomics (LASSO + Cox regression)	C-index for OS: 0.751 (95% CI: 0.661-0.841)	37/43
Park et al.[52]	Pancreas (PNET)	[18F] FDG PET/ CT	Detect risk of disease progression within 2 years.	N = 58	N/A	Clinical features + Radiomics (NN)	AUC: 0.83 (95% CI: 0.73-0.93). SENS: 0.78, SPEC: 0.77.	33/42
Pavel et al. [90]	NET Liver METS	CE- CT	Predict RFS	N = 138	N/A	Deep learning (ResNet50)	C-index (12 weeks): 0.66, C-index (24 weeks): 0.70.	34/41
Blazevic et al.[91]	SB-NETs	CE- CT	Predict intestinal complications (3 years)	N = 68 (100 random-split CV)	N/A	Radiomics (WORC)	AUC: 0.81 (95% CI: 0.72-0.91), SENS: 0.78, SPEC: 0.67	28/41

Acc, accuracy; AUC-ROC, area under the ROC curve; CE, contrast-enhanced; CT, computed tomography; CV, cross-validation; GEP, gastroenteropancreatic; GNEN, gastric neuroendocrine neoplasms; LASSO, least absolute shrinkage and selection operator; METS, metastases; ML, machine learning; MRI, magnetic resonance imaging; N/A, not applicable; NET, neuroendocrine tumor; NC, noncontrast; NN, neural network; OS, overall survival; PDAC, pancreatic ductal adenocarcinoma; PNET, pancreatic neuroendocrine tumors; PRRT: peptide receptor radionuclide therapy; RFS, recurrence-free survival; SB, small bowel; SENS, sensitivity; SPEC, specificity; SSA, somatostatin analogs; WORC, Workflow for Optimal Radiomics Classification.

*Summary metrics from the highest preforming model reported in the least biased cohort evaluated (i.e., cross-validation results, independent test set, external validation).

†CLAIM, checklist for artificial intelligence in medical imaging.[70,71] Evaluated a total of 44 items (CLAIM 2024), reported as number of observed items over the total number of possible categories, excluding N/A items.

straightforward integration of multimodal information. For such heterogeneous clinical entities, integrating multimodal information could enhance the ability of AI to analyze complex datasets, leading to improved diagnostic accuracy and a deeper understanding of NEN biology. The implementation of AI technologies in the future can aid meet the increasing workload requirements of radiology and nuclear medicine specialists. By leveraging AI-driven insights alongside expert clinical judgment, a synergistic approach emerges to address the challenges associated with the diagnosis and characterization of NENs. These innovations hold promise, but overcoming current challenges is essential to unlock the full potential of AI applications.

Conclusions

AI holds immense promise in revolutionizing the diagnosis, characterization, and management of neuroendocrine neoplasms. By integrating advanced imaging techniques, predictive analytics, and workflow optimization, AI enhances clinical decision-making and paves the way for personalized medicine. These tools can enhance classification accuracy, support the diagnosticians by reducing diagnostic uncertainty, and provide more reliable assessments to guide treatment planning. Despite challenges in standardization, validation, and limited training data due to the rarity of the disease, ongoing advancements in AI methodologies are set to transform management of neuroendocrine neoplasms, improving patient outcomes through more precise and efficient care.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Linda Chu reports financial support was provided by Lustgarten Foundation. Felipe Lopez-Ramirez reports financial support was provided by Lustgarten Foundation. Mohammad Yasrab reports financial support was provided by Lustgarten Foundation. Florent Tixier reports financial support was provided by Lustgarten Foundation. Satomi Kawamoto reports financial support was provided by Lustgarten Foundation. Elliot Fishman reports financial support was provided by Lustgarten Foundation. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Felipe Lopez-Ramirez: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Mohammad Yasrab:** Data curation, Writing – review & editing. **Florent Tixier:** Data curation, Writing – review & editing. **Satomi Kawamoto:** Writing – review & editing. **Elliot K. Fishman:** Conceptualization, Funding acquisition, Writing – review & editing. **Linda C. Chu:** Conceptualization, Supervision, Writing – review & editing.

References

1. Sultana Q, Kar J, Verma A, et al: A comprehensive review on neuroendocrine neoplasms: Presentation, pathophysiology and management. JCM 12(15):5138, 2023. https://doi.org/10.3390/jcm12155138
2. Hofland J, Kaltsas G, De Herder WW: Advances in the diagnosis and management of well-differentiated neuroendocrine neoplasms. EndocRev 41(2):371, 2020. https://doi.org/10.1210/endrev/bnz004
3. Das S, Dasari A: Epidemiology, incidence, and prevalence of neuroendocrine neoplasms: Are there global differences? Curr Oncol Rep 23 (4):43, 2021. https://doi.org/10.1007/s11912-021-01029-7
4. Lee MR, Harris C, Baeg KJ, et al: Incidence trends of gastroenteropancreatic neuroendocrine tumors in the united states. Clin Gastroenterol Hepatol 17 (11):2212, 2019. https://doi.org/10.1016/j.cgh.2018.12.017
5. Johnbeck CB, Mortensen J: Somatostatin receptor imaging PET in neuroendocrine neoplasm. PET Clin 16(2):191, 2021. https://doi.org/10.1016/j.cpet.2020.12.011
6. Hope TA, Allen-Auerbach M, Bodei L, et al: SNMMI procedure standard/EANM practice guideline for SSTR PET: Imaging neuroendocrine tumors. J Nucl Med 64(2):204-210, 2023. https://doi.org/10.2967/jnumed.122.264860
7. Adnan A, Basu S: Somatostatin receptor targeted PET-CT and its role in the management and theranostics of gastroenteropancreatic neuroendocrine neoplasms. Diagnostics 13(13):2154, 2023. https://doi.org/10.3390/diagnostics13132154
8. Chan DL, Hayes AR, Karfis I, et al: Dual [68Ga]DOTATATE and [18F] FDG PET/CT in patients with metastatic gastroenteropancreatic neuroendocrine neoplasms: A multicentre validation of the NETPET score. Br J Cancer 128(4):549-555, 2023. https://doi.org/10.1038/s41416-022-02061-5
9. Ambrosini V, Caplin M, Castaño JP, et al: Use and perceived utility of [18 F]FDG PET/CT in neuroendocrine neoplasms: A consensus report from the european neuroendocrine tumor society (ENETS) advisory board meeting 2022. J Neuroendocrinol 36(1):e13359, 2024. https://doi.org/10.1111/jne.13359
10. Ursprung S, Zhang ML, Asmundo L, et al: An illustrated review of the recent 2019 world health organization classification of neuroendocrine neoplasms: A radiologic and pathologic correlation. J Comput Assist Tomogr 48 (4):601-613, 2024. https://doi.org/10.1097/RCT.0000000000001159
11. Pantelis AG, Panagopoulou PA, Lapatsanis DP: Artificial intelligence and machine learning in the diagnosis and management of gastroenteropancreatic neuroendocrine neoplasms—a scoping review. Diagnostics (Basel) 12(4):874, 2022. https://doi.org/10.3390/diagnostics12040874
12. Park HJ, Kim HJ, Kim KW, et al: Comparison between neuroendocrine carcinomas and well-differentiated neuroendocrine tumors of the pancreas using dynamic enhanced CT. Eur Radiol 30(9):4772-4782, 2020. https://doi.org/10.1007/s00330-020-06867-w
13. Isensee F, Jaeger PF, Kohl SAA, et al: nnU-net: A self-configuring method for deep learning-based biomedical image segmentation. Nat Methods 18(2):203-211, 2021. https://doi.org/10.1038/s41592-020-01008-z
14. Erickson BJ, Korfiatis P, Akkus Z, et al: Machine learning for medical imaging. Radiographics 37(2):505-515, 2017. https://doi.org/10.1148/rg.2017160130
15. Gillies RJ, Kinahan PE, Radiomics Hricak H: Images are more than pictures, they are data. Radiology 278(2):563-577, 2016. https://doi.org/10.1148/radiol.2015151169
16. Kumar V, Gu Y, Basu S, et al: Radiomics: The process and the challenges. Magnet Reson Imaging 30(9):1234-1248, 2012. https://doi.org/10.1016/j.mri.2012.06.010

17. Cheng Phillip M, Montagnon Emmanuel, Yamashita Rikiya, et al: Deep learning: An update for radiologists. RadioGraphics 41(5):1427-1445, 2021. https://doi.org/10.1148/rg.2021200210
18. Soenksen LR, Ma Y, Zeng C, et al: Integrated multimodal artificial intelligence framework for healthcare applications. NPJ Digit Med 5:149, 2022. https://doi.org/10.1038/s41746-022-00689-4
19. Kora R, Mohammed A: A comprehensive review on transformers models for text classification. In: 2023 International Mobile, Intelligent, and Ubiquitous Computing Conference (MIUCC):1-7, 2023. https://doi.org/10.1109/MIUCC58832.2023.10278387
20. Ding W, Yu J, Zheng C, et al: Machine learning-based noninvasive quantification of single-imaging session dual-tracer 18F-FDG and 68Ga-DOTATATE dynamic PET-CT in oncology. IEEE Transact Med Imaging 41(2):347-359, 2022. https://doi.org/10.1109/TMI.2021.3112783
21. Seyyedi N, Ghafari A, Seyyedi N, et al: Deep learning-based techniques for estimating high-quality full-dose positron emission tomography images from low-dose scans: A systematic review. BMC Med Imaging 24(1):238, 2024. https://doi.org/10.1186/s12880-024-01417-y
22. Gong K, Berg E, Cherry SR, et al: Machine learning in PET: From photon detection to quantitative image reconstruction. In: In: Proceedings of the IEEE, 108:51-68, 2020. https://doi.org/10.1109/JPROC.2019.2936809
23. Katsari K, Penna D, Arena V, et al: Artificial intelligence for reduced dose 18F-FDG PET examinations: A real-world deployment through a standardized framework and business case assessment. EJNMMI Phys 8:25, 2021. https://doi.org/10.1186/s40658-021-00374-7
24. Xu J, Gong E, Pauly JM, et al. 200x low-dose PET reconstruction using deep learning. CoRR abs/1712.04119, 2017. doi: 10.48550/arXiv.1712.04119.
25. Arabi H, AkhavanAllaf A, Sanaat A, et al: The promise of artificial intelligence and deep learning in PET and SPECT imaging. Physica Medica 83:122-137, 2021. https://doi.org/10.1016/j.ejmp.2021.03.008
26. Balaji V, Song T, Malekzadeh M, et al: Artificial intelligence for PET and SPECT image enhancement. J Nucl Med 65(1):4, 2023. https://doi.org/10.2967/jnumed.122.265000
27. Weyts K, Lasnon C, Ciappuccini R, et al: Artificial intelligence-based PET denoising could allow a two-fold reduction in [18F]FDG PET acquisition time in digital PET/CT. Eur J Nucl Med Mol Imaging 49 (11):3750-3760, 2022. https://doi.org/10.1007/s00259-022-05800-1
28. Chaudhari AS, Mittra E, Davidzon GA, et al: Low-count whole-body PET with deep learning in a multicenter and externally validated study. NPJ Digit Med 4(1):1-11, 2021. https://doi.org/10.1038/s41746-021-00497-2
29. Loft M, Ladefoged CN, Johnbeck CB, et al: An investigation of lesion detection accuracy for artificial intelligence-based denoising of low-dose 64Cu-DOTATATE PET imaging in patients with neuroendocrine neoplasms. J Nucl Med 64(6):951-959, 2023. https://doi.org/10.2967/jnumed.122.264826
30. Hu M, Qian J, Pan S, et al: Advancing medical imaging with language models: Featuring a spotlight on ChatGPT. Phys Med Biol 69 (10):10TR01, 2024. https://doi.org/10.1088/1361-6560/ad387d
31. Akinci D'Antonoli T, Stanzione A, Bluethgen C, et al: Large language models in radiology: Fundamentals, applications, ethical considerations, risks, and future directions. Diagn Interv Radiol 30(2):80-90, 2024. https://doi.org/10.4274/dir.2023.232417
32. Choi H, Lee D, Kang Y. Empowering PET imaging reporting with retrieval-augmented large language models and reading reports database: A pilot single center study. 2024. doi: 10.1101/2024.05.13.24307312.
33. Lopez-Ramirez F, Soleimani S, Azadi JR, et al: Radiomics machine learning algorithm facilitates detection of small pancreatic neuroendocrine tumors on CT. Diagnost Intervent Imaging 106(1):28-40, 2025. https://doi.org/10.1016/j.diii.2024.08.003
34. Shin SY, Shen TC, Wank SA, et al: Fully-automated detection of small bowel carcinoid tumors in CT scans using deep learning. Med Phys 50 (12):7865-7878, 2023. https://doi.org/10.1002/mp.16391
35. Huang B, Lin X, Shen J, et al: Accurate and feasible deep learning based semi-automatic segmentation in CT for radiomics analysis in pancreatic neuroendocrine neoplasms. IEEE J Biomed Health Inform 25(9):3498-3506, 2021. https://doi.org/10.1109/JBHI.2021.3070708
36. Cao K, Xia Y, Yao J, et al: Large-scale pancreatic cancer detection via non-contrast CT and deep learning. Nat Med 29(12):3033-3043, 2023. https://doi.org/10.1038/s41591-023-02640-w
37. Geppert J, Asgharzadeh A, Brown A, et al: Software using artificial intelligence for nodule and cancer detection in CT lung cancer screening: Systematic review of test accuracy studies. Thorax 79(11):1040-1049, 2024. https://doi.org/10.1136/thorax-2024-221662
38. Park HJ, Shin K, You M, et al: Deep learning−based detection of solid and cystic pancreatic neoplasms at contrast-enhanced CT. Radiology 306(1):140-149, 2023. https://doi.org/10.1148/radiol.220171
39. Abi Nader C, Vetil R, Wood LK, et al: Automatic detection of pancreatic lesions and main pancreatic duct dilatation on portal venous CT scans using deep learning. Invest Radiol 58(11):791-798, 2023. https://doi.org/10.1097/RLI.0000000000000992
40. Wasserthal J, Breit H, Meyer MT, et al: TotalSegmentator: Robust segmentation of 104 anatomic structures in CT images. Radiol Artific Intell 5(5):e230024, 2023. https://doi.org/10.1148/ryai.230024
41. Fehrenbach U, Xin S, Hartenstein A, et al: Automatized hepatic tumor volume analysis of neuroendocrine liver metastases by GD-EOB MRI—A deep-learning model to support multidisciplinary cancer conference decision-making. Cancers 13(11):2726, 2021. https://doi.org/10.3390/cancers13112726
42. Haque F, Carrasquillo JA, Turkbey EB, et al: An automated pheochromocytoma and paraganglioma lesion segmentation AI-model at whole-body 68Ga- DOTATATE PET/CT. EJNMMI Res 14(1):103, 2024. https://doi.org/10.1186/s13550-024-01168-5
43. Carlsen EA, Lindholm K, Hindsholm A, et al: A convolutional neural network for total tumor segmentation in [64Cu]cu-DOTATATE PET/CT of patients with neuroendocrine neoplasms. EJNMMI Res 12:30, 2022. https://doi.org/10.1186/s13550-022-00901-2
44. Staal FCR, Aalbersberg EA, Van Der Velden D, et al: GEP-NET radiomics: A systematic review and radiomics quality score assessment. Eur Radiol 32(10):7278-7294, 2022. https://doi.org/10.1007/s00330-022-08996-w
45. Yan Q, Chen Y, Liu C, et al: Predicting histologic grades for pancreatic neuroendocrine tumors by radiologic image-based artificial intelligence: A systematic review and meta-analysis. Front Oncol 14:1332387, 2024. https://doi.org/10.3389/fonc.2024.1332387
46. Azoulay A, Cros J, Vullierme M, et al: Morphological imaging and CT histogram analysis to differentiate pancreatic neuroendocrine tumor grade 3 from neuroendocrine carcinoma. Diagnost Intervent Imaging 101(12):821-830, 2020. https://doi.org/10.1016/j.diii.2020.06.006
47. Gu X, Cui Y, Zhu H, et al: Discrimination of liver metastases of digestive system neuroendocrine tumors from neuroendocrine carcinoma by computed tomography−Based radiomics analysis. J Comput Assist Tomogr 47(3):361, 2023. https://doi.org/10.1097/RCT.0000000000001443
48. Bevilacqua A, Calabrò D, Malavasi S, et al: A [68Ga]ga-DOTANOC PET/CT radiomic model for non-invasive prediction of tumour grade in pancreatic neuroendocrine tumours. Diagnostics 11(5):870, 2021. https://doi.org/10.3390/diagnostics11050870
49. Liao T, Su T, Lu Y, et al: Random survival forest algorithm for risk stratification and survival prediction in gastric neuroendocrine neoplasms. Sci Rep. 14(1):26969, 2024. https://doi.org/10.1038/s41598-024-77988-1
50. Mapelli P, Partelli S, Salgarello M, et al: Dual tracer 68Ga-DOTATOC and 18F-FDG PET/computed tomography radiomics in pancreatic neuroendocrine neoplasms: An endearing tool for preoperative risk assessment. Nucl Med Commun 41(9):896-905, 2020. https://doi.org/10.1097/MNM.0000000000001236
51. Atkinson C, Ganeshan B, Endozo R, et al: Radiomics-based texture analysis of 68Ga-DOTATATE positron emission tomography and computed tomography images as a prognostic biomarker in adults with neuroendocrine cancers treated with 177Lu-DOTATATE. Front Oncol 11:686235, 2021. https://doi.org/10.3389/fonc.2021.686235
52. Park Y, Park YS, Kim ST, et al: A machine learning approach using [18F]FDG PET-based radiomics for prediction of tumor grade and prognosis in pancreatic neuroendocrine tumor. Mol Imaging Biol 25(5):897-910, 2023. https://doi.org/10.1007/s11307-023-01832-7

53. Gadens Zamboni C, Dundar A, Jain S, et al: Inter- and intra-tumoral heterogeneity on [68Ga]ga-DOTA-TATE/[68Ga]ga-DOTA-TOC PET/CT predicts response to [177Lu]lu-DOTA-TATE PRRT in neuroendocrine tumor patients. EJNMMI Rep 8(1):39, 2024. https://doi.org/10.1186/s41824-024-00227-3
54. Behmanesh B, Abdi-Saray A, Deevband MR, et al: Predicting the response of patients treated with 177Lu-DOTATATE using single-photon emission computed tomography−computed tomography image-based radiomics and clinical features. J Med Signals Sens 14:28, 2024. https://doi.org/10.4103/jmss.jmss_54_23
55. Bilgin GB, Bilgin C, Burkett BJ, et al: Theranostics and artificial intelligence: New frontiers in personalized medicine. Theranostics 14 (6):2367, 2024. https://doi.org/10.7150/thno.94788
56. Dewaraja YK, Mirando DM, Peterson AB, et al: A pipeline for automated voxel dosimetry: Application in patients with multi-SPECT/CT imaging after 177Lu-peptide receptor radionuclide therapy. J Nucl Med 63 (11):1665-1672, 2022. https://doi.org/10.2967/jnumed.121.263738
57. Akhavanallaf A, Peterson AB, Fitzpatrick K, et al: The predictive value of pretherapy [68Ga]ga-DOTA-TATE PET and biomarkers in [177Lu]lu-PRRT tumor dosimetry. Eur J Nucl Med Mol Imaging 50(10):2984-2996, 2023. https://doi.org/10.1007/s00259-023-06252-x
58. Plachouris D, Eleftheriadis V, Nanos T, et al: A radiomic- and dosiomic-based machine learning regression model for pretreatment planning in 177Lu-DOTATATE therapy. Medical Physics 50(11):7222, 2023. https://doi.org/10.1002/mp.16746
59. Wehrend J, Silosky M, Xing F, et al: Automated liver lesion detection in 68Ga DOTATATE PET/CT using a deep fully convolutional neural network. EJNMMI Res 11(1):98, 2021. https://doi.org/10.1186/s13550-021-00839-x
60. Shen K, Su W, Liang C, et al: Differentiating small. Eur Radiol 34 (12):7553-7563, 2024. https://doi.org/10.1007/s00330-024-10837-x
61. Liu X, Li H, Wang S, et al: CT radiomics to differentiate neuroendocrine neoplasm from adenocarcinoma in patients with a peripheral solid pulmonary nodule: A multicenter study. Front Oncol 14:1420213, 2024. https://doi.org/10.3389/fonc.2024.1420213
62. Shi Y, Zhu H, Li X, et al: Histogram array and convolutional neural network of DWI for differentiating pancreatic ductal adenocarcinomas from solid pseudopapillary neoplasms and neuroendocrine neoplasms. Clin Imaging 96:15-22, 2023. https://doi.org/10.1016/j.clinimag.2023.01.008
63. Cao, Wang, Ren, et al: Differentiation of retroperitoneal paragangliomas and schwannomas based on computed tomography radiomics. Sci Rep. 13:9253, 2023. https://doi.org/10.1038/s41598-023-28297-6
64. Zhang T, Xiang Y, Wang H, et al: Radiomics combined with multiple machine learning algorithms in differentiating pancreatic ductal adenocarcinoma from pancreatic neuroendocrine tumor: More hands produce a stronger flame. J Clin Med 11(22):6789, 2022. https://doi.org/10.3390/jcm11226789
65. Chu LC, Park S, Soleimani S, et al: Classification of pancreatic cystic neoplasms using radiomic feature analysis is equivalent to an experienced academic radiologist: A step toward computer-augmented diagnostics for radiologists. Abdom Radiol 47(12):4139, 2022
66. Han X, Yang J, Luo J, et al: Application of CT-based radiomics in discriminating pancreatic cystadenomas from pancreatic neuroendocrine tumors using machine learning methods. Front Oncol 11:606677, 2021. https://doi.org/10.3389/fonc.2021.606677
67. Shi Y, Zhu H, Liu Y, et al: Radiomics analysis based on diffusion kurtosis imaging and T2 weighted imaging for differentiation of pancreatic neuroendocrine tumors from solid pseudopapillary tumors. Front Oncol 10:1624, 2020. https://doi.org/10.3389/fonc.2020.01624
68. Yi X, Guan X, Zhang Y, et al: Radiomics improves efficiency for differentiating subclinical pheochromocytoma from lipid-poor adenoma: A predictive, preventive and personalized medical approach in adrenal incidentalomas. EPMA J 9(4):421-429, 2018. https://doi.org/10.1007/s13167-018-0149-3
69. Santilli A, Panyam P, Autz A, et al: Automated full body tumor segmentation in DOTATATE PET/CT for neuroendocrine cancer patients. Int J CARS 18(11):2083-2090, 2023. https://doi.org/10.1007/s11548-023-02968-1
70. Tejani AS, Klontzas ME, Gatti AA, et al: Checklist for artificial intelligence in medical imaging (CLAIM): 2024 update. Radiol Artific Intell 6 (4):e240300, 2024. https://doi.org/10.1148/ryai.240300
71. Mongan J, Moy L, Kahn J, et al: Checklist for artificial intelligence in medical imaging (CLAIM): A guide for authors and reviewers. Radiol Artific Intell 2(2):e200029, 2020. https://doi.org/10.1148/ryai.2020200029
72. Tixier F, Lopez-Ramirez F, Blanco A, et al: Can CT image reconstruction parameters impact the predictive value of radiomics features in grading pancreatic neuroendocrine neoplasms? Bioengineering 12(1):80, 2025. https://doi.org/10.3390/bioengineering12010080
73. Ye J, Fang P, Peng Z, et al: A radiomics-based interpretable model to predict the pathological grade of pancreatic neuroendocrine tumors. Eur Radiol 34(3):1994-2005, 2024. https://doi.org/10.1007/s00330-023-10186-1
74. Ahmed TM, Zhu Z, Yasrab M, et al: Preoperative prediction of lymph node metastases in nonfunctional pancreatic neuroendocrine tumors using a combined CT Radiomics−Clinical model. Ann Surg Oncol 31 (12):8136-8145, 2024. https://doi.org/10.1245/s10434-024-16064-4
75. Mapelli P, Bezzi C, Muffatti F, et al: Preoperative assessment of lymph nodal metastases with [68Ga]ga-DOTATOC PET radiomics for improved surgical planning in well-differentiated pancreatic neuroendocrine tumours. Eur J Nucl Med Mol Imaging 51(9):2774-2783, 2024. https://doi.org/10.1007/s00259-024-06730-w
76. Gu W, Chen Y, Zhu H, et al: Development and validation of CT-based radiomics deep learning signatures to predict lymph node metastasis in non-functional pancreatic neuroendocrine tumors: A multicohort study. eClinicalMedicine 65:102269, 2023. https://doi.org/10.1016/j.eclinm.2023.102269
77. Javed AA, Zhu Z, Kinny-Köster B, et al: Accurate non-invasive grading of nonfunctional pancreatic neuroendocrine tumors with a CT derived radiomics signature. Diagnost Intervent Imaging 105(1):33-39, 2024. https://doi.org/10.1016/j.diii.2023.08.002
78. Mori M, Palumbo D, Muffatti F, et al: Prediction of the characteristics of aggressiveness of pancreatic neuroendocrine neoplasms (PanNENs) based on CT radiomic features. Eur Radiol 33(6):4412-4421, 2023. https://doi.org/10.1007/s00330-022-09351-9
79. Liu C, Bian Y, Meng Y, et al: Preoperative prediction of G1 and G2/3 grades in patients with nonfunctional pancreatic neuroendocrine tumors using multimodality imaging. Acad Radiol 29(4):e49-e60, 2022. https://doi.org/10.1016/j.acra.2021.05.017
80. Wang X, Qiu J, Tan C, et al: Development and validation of a novel radiomics-based nomogram with machine learning to preoperatively predict histologic grade in pancreatic neuroendocrine tumors. Front Oncol 12:843376, 2022. https://doi.org/10.3389/fonc.2022.843376
81. Zhang T, Zhang Y, Liu X, et al: Application of radiomics analysis based on CT combined with machine learning in diagnostic of pancreatic neuroendocrine tumors patient's pathological grades. Front Oncol 10:521831, 2020. https://doi.org/10.3389/fonc.2020.521831
82. Luo Y, Chen X, Chen J, et al: Preoperative prediction of pancreatic neuroendocrine neoplasms grading based on enhanced computed tomography imaging: Validation of deep learning with a convolutional neural network. Neuroendocrinology 110(5):338-350, 2020. https://doi.org/10.1159/000503291
83. Bian Y, Zhao Z, Jiang H, et al: Noncontrast radiomics approach for predicting grades of nonfunctional pancreatic neuroendocrine tumors. J Magn Reson Imaging 52(4):1124-1136, 2020. https://doi.org/10.1002/jmri.27176
84. Zhao Z, Bian Y, Jiang H, et al: CT-radiomic approach to predict G1/2 nonfunctional pancreatic neuroendocrine tumor. Acad Radiol 27(12):e272-e281, 2020. https://doi.org/10.1016/j.acra.2020.01.002
85. Polici M, Caruso D, Masci B, et al: Radiomics in advanced gastroentero-pancreatic neuroendocrine neoplasms: Identifying responders to somatostatin analogs. J Neuroendocrinol 37(1):e13472, 2025. https://doi.org/10.1111/jne.13472
86. Heo S, Park HJ, Kim HJ, et al: Prognostic value of CT-based radiomics in grade 1-2 pancreatic neuroendocrine tumors. Cancer Imaging 24 (1):28, 2024. https://doi.org/10.1186/s40644-024-00673-z
87. Behmanesh B, Abdi-Saray A, Deevband MR, et al: Radiomics analysis for clinical decision support in 177Lu-DOTATATE therapy of metastatic

neuroendocrine tumors using CT images. J Biomed Phys Eng 14 (5):423-434, 2024. https://doi.org/10.31661/jbpe.v0i0.2112-1444

88. Homps M, Soyer P, Coriat R, et al: A preoperative computed tomography radiomics model to predict disease-free survival in patients with pancreatic neuroendocrine tumors. Eur J Endocrinol 189(4):476-484, 2023. https://doi.org/10.1093/ejendo/lvad130
89. Yang Z, Han Y, Cheng M, et al: Prognostic value of computed tomography radiomics features in patients with gastric neuroendocrine neoplasm. Front Oncol 13:1143291, 2023. https://doi.org/10.3389/fonc.2023.1143291
90. Pavel M, Dromain C, Ronot M, et al: The use of deep learning models to predict progression-free survival in patients with neuroendocrine tumors. Future Oncol 19(32):2185-2199, 2023. https://doi.org/10.2217/fon-2022-1136
91. Blazevic A, Starmans MPA, Brabander T, et al: Predicting symptomatic mesenteric mass in small intestinal neuroendocrine tumors using radiomics. Endocr Relat Cancer 28(8):529-539, 2021. https://doi.org/10.1530/ERC-21-0064