AI potential in PET/CT cancer imaging

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Keywords: Artificial intelligence - Cancer - Deep learning - Machine learning - PET - Radiomics

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Received:
17 September 2024
Accepted revised:
22 November 2024

Abstract
Positron emission tomography/computed tomography (PET/CT) is a hybrid medical imaging technique that combines PET and CT to provide detailed images of the body's anatomical structures and metabolic activity. It is frequently used for oncology and other medical diagnoses. This overview aims to examine how artificial intelligence (AI) has been used in PET/CT, based on recent state-of-art. There are a number of clinical questions in Nuclear Medicine, and AI could provide answers, having the capability to enhance various aspects of medical imaging. The overview focuses on how machine learning (ML) and deep learning (DL), enhance tumor segmentation, classification, diagnosis, disease-free survival prediction and treatment response prediction in oncology. The analysis showed that the application of AI provides reliable results, especially in the fields of classification and diagnosis. In addition, radiomics is a novel research field enabling quantitative analysis of medical images through feature extraction, utilized for AI model implementation. Despite these advances, addressing issues such as dataset size, standardization, and ethical concerns are essential for broad clinical integration of AI in PET/CT oncology imaging.

Hell J Nucl Med 2024; 27(3): 212-221 *Epub ahead of print: 14 December 2024* *Published online: 30 December 2024*

Introduction

Positron emission tomography (PET) is a three-dimensional (3D) functional imaging modality that can offer important insights into the diagnosis and treatment of cancer patients [1, 2]. It involves visualizing the bio-distribution of radiopharmaceuticals labeled with positron-emitting radionuclides and diagnosing physiological/pathological conditions [3, 4]. It provides the ability to examine various changes in metabolism, blood flow, and regional chemical composition [4]. Researchers now have a better understanding of the metabolic and molecular processes involved in the disease thanks to the radiopharmaceuticals used in PET. As a result, PET is now a molecular imaging technique that examines biochemical processes at the molecular level [4]. Positron emission tomography imaging has been used in many different types of malignant diseases due to the benefits of revealing tumor cells' functional status and molecular expression [5].

On the other hand, computed tomography (CT) scans are produced by converting electrical energy (moving electrons) into X-rays photons, sending them through the target being examined, measuring the photons, and then converting the electrons from measured photons. The degree of penetration depends on its density. X-rays beams passing through an anatomy section can reveal information about that area. The CT image is then computationally reconstructed by the collected data [6].

In the field of medical diagnostics, healthcare professionals can take advantage of both techniques, PET and CT, by combining PET and CT scans into a single image examination, as PET/CT, allowing a more thorough examination of various diseases, particularly cancer [7]. By combining the data, CT and PET can both highlight areas of abnormal metabolism and localize functional abnormalities precisely [8] and this process is known as hybrid imaging [9].

Nuclear medicine imaging, and therefore PET/CT imaging, does have some well-known drawbacks, which limit its clinical use. Despite the diagnostic value of PET/CT, challenges such as interobserver variability, large data processing, and lack of time have led to increased interest in the use of artificial intelligence (AI) in the field of medical imaging. Artificial intelligence and PET imaging may be able to help physicians to manage their patients in a significant way [9-11]. However, the ethical deployment and utilization of AI in healthcare necessitates consideration of ethical issues and data privacy concerns [11].

However, the increasing amount of medical imaging data also presents a challenge for accurate and efficient analysis. Herein lies the potential utility of AI [11].

When it comes to using PET imaging, there are a few constraints. Firstly, there are not enough tools for evaluating functions and describing PET images. Currently, the main methods used to describe the functional status are semi-quantitative parameters. Among them, maximum standardized uptake value (SUVmax) and mean SUV (SUVmean) are frequently used in clinical applications. They have a relationship with tumor grade and stage, and they are clinically useful for predicting prognosis and therapy response. This correlation is not widely accepted, and some studies continue to show dubious findings [12].

There is no standard cut-off value of semi-quantitative parameters to divide benign and malignant lesions. Additionally, inter-acquisition variation affects the stability of value. Semi-quantitative parameters cannot effectively extract information from PET images [5]. When it comes to diagnostic choices, given its complexity and heterogeneity, cancer is a condition that requires a precise diagnosis and treatment strategy. The detection, staging, and monitoring of tumors using PET/CT imaging are crucial for the management of cancer [13]. The integration of functional and anatomical information from PET/CT scans enables clinicians to evaluate tumor activity, identify potential metastases, and evaluate treatment effectiveness [14]. When it comes to diagnostic choices, given its complexity and heterogeneity, cancer is a condition that requires a precise diagnosis and treatment strategy. The detection, staging, and monitoring of tumors using PET/CT imaging are crucial for the management of cancer. The integration of functional and anatomical information from PET/CT scans enables clinicians to evaluate tumor activity, identify potential metastases, and evaluate treatment effectiveness [12]. However, the increasing amount of medical imaging data also presents a significant challenge for accurate and efficient analysis. Herein lies the potential utility of AI [13].

Artificial intelligence is the science of creating algorithms that can learn from data to solve specific problems. Although it is associated with the task of employing computers to comprehend human intelligence, AI does not need to be limited to techniques that can be observed biologically [15].

Several aspects of medical imaging can be enhanced by AI. In addition to improving quality assessment, it can also be useful in post-processing techniques like tumor delineation, registration, and quantification and clinical decision support [2, 16]. Additionally, it can contribute to the optimization of dose estimation, automating abnormality detection, comparing with earlier examinations, and evaluating therapeutic response, interpreting and generating reports, and correlating findings with other clinical data [2, 16]. All the aforementioned are benefits of AI for PET/CT as a diagnostic imaging modality. Thus, the procedure will be more precise and faster [2].

Tumor characterization and image analysis have undergone radical changes as a result of the significant advancements in AI techniques, including machine learning and deep learning [17]. This has resulted in remarkably better healthcare outcomes [18].

This overview intends to investigate how AI has been applied in order to address the main challenges related to PET/CT, with a focus on cancer imaging. The benefits from using AI in medical images presented include improvements in segmentation, classification, diagnosis, disease-free survival prediction, and treatment response prediction in the field of oncology.

Background concepts: Machine learning techniques for PET/CT analysis

Background of AI and terminology

Artificial intelligence focuses on creating systems and technologies that can perform tasks that typically demand human-like intelligence. These tasks can include problem solving, reading, reasoning, natural language processing, pattern recognition, and decision making [2, 16, 19]. Machine learning (ML) is a subset of AI that consists of multiple algorithms that allow computers to automatically perform these tasks. Machine learning involves developing algorithms and models that allow machines to learn from data. Machine learning systems are trained on large data sets and use statistical techniques to make predictions or decisions based on patterns and in-sights from that data [20].

Building an ML model requires several important steps and considerations, including the use of the training set, testing and validation, and the methods used to report the model's success. The training set is used to train the model. Algorithms learn how to make predictions or classify data based on this data set. The purpose of validation is to provide an objective assessment of the model's performance during training. Testing sets are used to evaluate the performance of a fully developed model and provide an objective assessment of its effectiveness [21].

Supervised learning refers to a category of ML where an algorithm is trained on a labeled dataset, meaning that each input in the training data is associated with the corresponding correct output. The objective is to teach the model to map inputs to outputs so that it can make accurate predictions on new data. Support vector machines (SVM) are a supervised machine learning algorithm used for classification and regression tasks. It identifies the optimal hyperplane in the feature space to effectively separate different classes [14]. Random forests, on the other hand, is an algorithm that constructs multiple decision trees during training and combines them for more precise and stable predictions [22].

Semi-supervised learning entails training a model on a dataset that includes both labeled and unlabeled examples. This approach is valuable when labeling data is time-consuming. Leveraging unlabeled data in can enhance the overall performance of the model [23].

Unsupervised learning uses ML algorithms to analyze and cluster unlabeled data sets. These algorithms are ideal for data exploration and image recognition [24].

Machine learning algorithms are mostly applied to extracted features (agnostic and/or semantic) with feature selection or dimensionally reduction and regression or classification steps. Deep learning (DL) is a subset of ML algorithms that performs not only all these ML steps (feature selection, dimensionally reduction, regression, or classification) but also features extraction in within the same framework [25, 26]. Deep learning is a subfield of machine learning that focuses on artificial neural networks inspired by the structure and function of the human brain. Deep learning has received much attention for its ability to solve problems such as image recognition, natural language processing, and autonomous decision making [27]. Deep learning is regarded as representation learning, which entails a collection of techniques that would allow a machine to be fed raw data and automatically identify the representation it needs for classification [28].

A convolutional neural network (CNN) is a specialized artificial neural network designed for the analysis and processing of visual data, particularly images. Convolutional neural networks utilize convolutional layers to autonomously learn and adaptively discern spatial hierarchies of features from the input data [29].

An auto-encoder is an artificial neural network employed in unsupervised learning. It comprises an encoder network that condenses the input data into a lower-dimensional representation (encoding), and a decoder network that reconstructs the input data from this encoding. Auto-encoders find applications in data compression, feature learning, and anomaly detection [30].

Transformers refer to a neural network architecture. They have gained widespread use in natural language processing (NLP) tasks, relying on mechanisms to process input data in parallel [31].

Reinforcement learning is a machine learning training method where an agent learns decision-making by interacting with an environment and receiving feedback in the form of rewards or penalties based on its actions [32].

Generative adversarial networks (GAN) are a class of machine learning models that consist of a generator and a discriminator, trained simultaneously through adversarial training. The generator produces synthetic data, and the discriminator evaluates the authenticity of the generated data. This iterative process continues until the generator produces data indistinguishable from real data [33].

Radiomics analysis

Radiomics is a term used to describe the high-capacity extraction, and analysis of numerous features from medical images. It is believed that medical images contain more information than the human eye can perceive, and that additional information may supplement the usual descriptive data available to health professionals [34].

Radiomics deals with the extraction of specific image features that enable the automated classification of medical images into specific categories [35]. Using quantitative indices derived from statistical and mathematical models applied to the images, radiomic features enable the description of structural heterogeneity of tissues, particularly referred to tumors [36].

Radiomics evaluate size, shape, and texture features that contain valuable spatial information about the distribution and pixel or voxel patterns as part of its analysis. These radiomics features are used to build predictive models for many different organs and systems, to order to support individualized diagnosis and treatment [37].

The radiomics image processing workflow entails a series of sequential steps. Starting from image acquisition and preprocessing, segmentation of the desired region of interest takes place, a process that is typically done manually. Then follows the calculation of defined radiomics features and creation of the classification model [37].

A. From raw data to segmentation: The medical image serves as the starting point for the radiomic workflow. A data set's pixel intensities are distributed uniformly and within a predetermined range using normalization techniques [38, 39]. The information that can be extracted is then limited to that which is relevant to the lesion, and this limited set of relevant information is referred to as the region of interest (ROI). Both in two dimensions and three dimensions, there are competing techniques for feature extraction.

The manual segmentation of the lesion can be accomplished using automated segmentation algorithms. Deep learning architectures like U-Net or semi-automatic techniques like click-and-grow algorithms are two examples of automated segmentation techniques [39, 40].

B. Calculating the radiomics features: Once the ROI has been established, the information sought will determine which features should be extracted. Shape features like volume only affect how the ROI is defined, and if this is done manually, there will be inter- and intra-observer variation. Variance, skewness, and kurtosis are just a few of the statistical techniques used to quantify the pixel intensity histograms. However, the positioning of pixels in relation to one another cannot be measured by these features. This relationship may be captured by second and higher order features, with second order features based on the average relationship between two pixels/voxels and higher order features for more than two pixels/voxels. The grey level co-occurring matrix (GLCM) is a prime example of a second-order feature extraction approach. The GLCM can then be used to extract independent features using customized formula and statistical analysis. As they are predefined by specially created formula, features extracted in this way are referred to as "handcrafted" features. One must choose the subset of them that will be used in the final model [39].

C. Radiomics challenges. Although, the repeatability, reproducibility, and transferability of radiomics features, despite the promising results and the potential of radiomics, is still a problem and frequently depends on the image characteristics. The extraction of radiomics features from multiple image acquisitions made with identical or nearly identical acquisition and processing parameters is a common method for evaluating repeatability. On the other hand, reproducibility of radiomics features, also known as robustness, is assessed when the measurement systems and acquisition parameters are different [41].

Machine learning and deep learning for medical imaging

By automating some tasks and assisting imagers in their de-

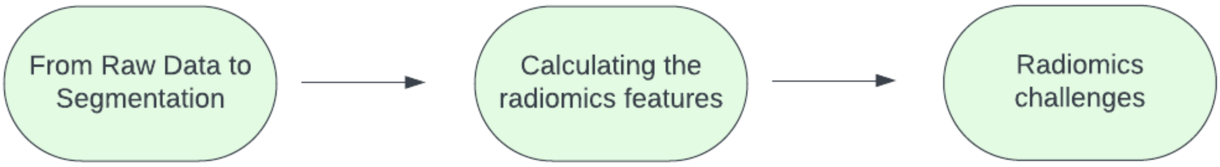

Figure 1. Radiomics image processing workflow.

cision-making, AI has the potential to improve the accuracy, efficacy, and reproducibility of PET/CT image analysis [42]. Machine learning algorithms are thought to automatically spot patterns and extract desirable representations from unstructured data [43, 44]. Machine learning algorithms are mos-tly applied to extracted features with feature selection or dimensionally reduction [25, 26]. Some common algorithms and methods that are used in the field of medical imaging are linear or logistic regression, decision trees and random forests, support vector machines [45].

Deep learning has shown promising results in a number of problems related to nuclear medicine, and various DL algorithms have been proposed and used [44, 46, 47]. Convolutional neural networks and GAN are among the DL algorithms used in nuclear medicine [25, 44, 48, 49] that have been used to recover low-quality images and produce high-quality images in the domain of medical imaging [50, 51].

As a method for understanding medical images, CNN has grown to be a potent option. Numerous medical images understanding applications have all been successfully implemented using CNN [52].

Generative adversarial networks are able to produce realistic images. They are the first deep generative models to be extensively used for medical image augmentation [53].

Moreover, applications of AI-based algorithms in PET imaging span from internal dosimetry at the highest levels to low-level electronic signal formation and processing, as well as diagnostic and prognostic modeling [44]. Deep learning strategies have been primarily used in instrumentation advancements to increase the timing resolution and localization accuracy of incident photons with the goal of improving the overall spatial and time-of-flight (TOF) resolutions in PET. With the rapid emergence of DL algorithms, image reconstruction algorithms are being reexamined. In these algorithms, ML models take the place of either all of the analytical models used in the image reconstruction process or certain crucial components [44].

Quality optimization for low-quality images is one of the main uses of DL in PET image reconstruction. The injection dose should be as low as possible to reduce radiation exposure to the examinee and medical personnel. Reducing the injection dose, however, worsens the image quality and increases noise in the PET acquisition data [51, 54, 55].

Recently, PET hardware has improved [51, 54, 55], and reconstruction has allowed us to lower the dose while preserving image quality [51, 56, 57]. However, there is still a sizable radiation exposure from PET scans [51]. The overall quality of PET scan subjects can still be improved with the use of strategies to mitigate the noise brought on by lowering the injection dose [51].

Methodology of literature search

A literature search was performed in order to provide an overview of how computational analysis and AI have been applied to PET/CT data in order to address the main challenges related to this type of hybrid imaging data. The selection of keywords ensured the thorough retrieval of research spanning the interdisciplinary field of medical image analysis. The methodology employed for conducting the literature search used the following keywords: artificial intelligence (AI), cancer, deep learning (DL), machine learning (ML), positron emission tomography (PET), positron emission tomography/computed tomography (PET/CT), radiomics. It is important to note that the "radiomics" keyword was employed because many ML research works were based on radiomics. The search aimed to find pertinent research papers and studies in the area.

The academic databases included in the search were PubMed, IEEE Xplore, and Google Scholar. These databases were chosen due to their coverage of technical and medical literature. The studies that were included covered the use of AI algorithms in medical image analysis.

The following queries were used for the literature search:

- ((AI)OR(machine learning)OR(deep learning))AND (cancer) AND(PET-CT) AND (radiomics) (Query 1)
- (((AI)OR(machine learning)OR (deep lear-ning)OR (radiomics))AND(cancer) AND(PET-CT))AND(classification)AND(free full text[Filter]))AND(review[Publication Type]) (Query 2)

The initial query was employed to explore and assess the scope of existing research within the field under examination. In the first query, "radiomics" is a mandatory term, required in all search results. In the second query, "radiomics" is an optional term, in order to also search for studies that do not use radiomics. In addition, the application of the second query was intended to incorporate review articles into the overview, because of the scarcity of original research articles (not review articles) that delved into the intersection of AI and classification.

The two queries returned the following number of articled: Query 1: 322 and Query 2: 14. Then the research was limited to the articles published over the past six years (2018-2023), resulting in a decrease in the volume of the obtained articles (Query 1: 318 and Query 2: 13). The reason for this limitation in article selection is due to the fact that AI has a significant development in recent years, necessitating the inclusion of more recent studies in the overview. Firstly, the abstracts were reviewed for relevance to the study goals, and certain articles were excluded in order to focus on those that align with AI models applied to PET/CT scans. Secondly, additional articles were excluded due to overlaps between the two queries. Consequently, this process resulted in the final collection of 12 articles (8 original articles form the Query 1 and 4 studies included in 1 review from Query 2.

Challenges of AI in cancer research

This overview investigates the intersection of AI and cancer research, using information from 12 studies, of which 8 were original research articles and the remaining 4 were studies derived from one review article. The studies covered the following clinical questions: segmentation, classification, diagnosis, disease-free survival prediction, and treatment response. Table 1 presents and organizes the essential information from the 8 studies pertaining to all previously mentioned questions, with the exception of classification. This exclusion is due to the fact that the percentages below pertain to the original research articles. In subsequent sections, more detailed information on these studies will be presented.

Automated segmentation

Segmentation can be done by drawing ROI on the tumor, tumor subregions (also known as "habitats"), or peritumoral zones [58]. For larger datasets where manual segmentation is not practical, automatic segmentation may be necessary [59, 60] because it is potentially faster and more reproducible. To make sure segmentations are accurate, a radiologist should review them. When manual segmentation is employed, feature stability should be evaluated by performing numerous delineations of the same tumor [60].

Ghezzo et al. (2023) study was about a convolutional neural network for the automatic segmentation of intraprostatic cancer lesions which was tested on 39 patients' PET/CT images [61].

In another study of Gu et al. (2023), a deep multi-task survival model (DeepMTS) was developed for tumor segmentation from fluorine-18-fluorodeoxyglucose (^{18}F-FDG) PET/CT images. The preprocessed PET and CT images were combined and sent as input to DeepMTS, and the original manual tumor segmentation mask was used as the ground truth label for training only. DeepMTS is a CNN consisting of a Unet-based segmentation backbone and a DenseNet-based cascading survival network (CSN) [62].

After training, DeepMTS can predict the segmentation mask of the tumor region. For tumor segmentation, Deep MTS achieves dimensional similarity coefficients (DSC) of 0.826, 0.775, and 0.765 for the training, internal validation, and external validation cohorts, respectively, demonstrating high agreement with manually segmented segmentation masks. Automatic segmentation has been reported to increase objectivity and significantly improve prediction per-

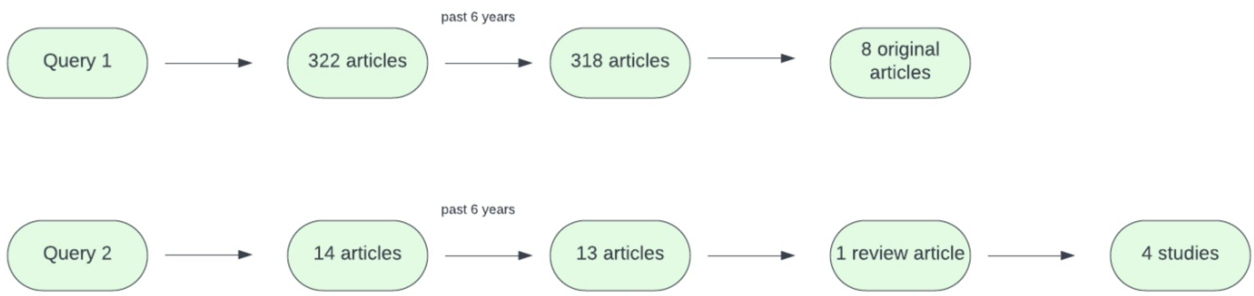

Figure 2. Flow chart of article selection process

Table 1. Key information of the overview: insights from 8 studies.

AI subset	ML: 62.5%	DL: 37.5%		
Radiomics utilization	Yes: 87.5 %	No: 12.5%		
Cancer type	Lung cancer: 37.5%	Prostate cancer: 25%	Cervical cancer: 25%	Nasopharyngeal carcinoma: 12.5%
Clinical question	Segmentation: 25%	Diagnosis: 25%	Disease-free survival prediction: 25%	Treatment response: 25%

formance compared to manual segmentation [62].

Classification of lesions

Classification is the categorization of a population [63]. The choice of classification algorithm significantly impacts the variability in the predictive performance of machine learning models [64]. Predictive models use clinical outcomes to group patients into various risk groups based on the likelihood that clinical outcomes, such as overall or disease-free survival, will occur. These risk groups are then evaluated using a time-to-event analysis. The idea that radiomic data provide information about tumor biology informs these applications [63].

At Moazemi et al. (2021) study, 5 different ML models have been tested for classification of lesions in patients that had been treated for either localized or metastasized prostate cancer and referred for a follow-up PET/CT. Lesions were delineated by physicians and features (from PET and from CT) were calculated from each lesion and utilized in each algorithm, with an ExtraTrees classifier showing the best results (AUC 0.98, sensitivity 94%, and specificity 89%). The results showed that the combination of PET and CT features greatly improved the classification accuracy [65].

In a similar study, Erle et al. (2021) tested three different ML radiomics models based on support vector machine, ExtraTrees and random forest models, respectively. The aim of the study was the classification between malignant and physiological findings. A lot of hotspots were delineated and marked either as malignant or physiological. The ExtraTree classifier showed the best results [66].

Leung et al. (2022) study developed a radiomics model for classification in prostate cancer cases. A deep learning approach was used for automated segmentation of lesions and extracting features (AUC 0.90) [67].

The study of Zang et al. (2022) developed a radiomics model for classification of malignant and benign findings at prostate disease. For the purpose of the study, they developed a radiomics model score constructed by a linear combination of coefficients from a selection of radiomic features [68].

Table 2. *Performance of studies for segmentation.*

Study	# of patients	Cancer type	Radiopharma-ceutical	Assessment measures	AI subset	Radiomics utilization
Ghezzo et al. [61]	39	Prostate cancer	^{68}Ga-PSMA	Median dice score = 0.74	DL	No
Gu et al. [62]	886	Nasopharyngeal carcinoma	^{18}F-FDG	DSC = 0.826 (for the training) DSC = 0.775 (for the internal validation) DSC = 0.765 (for the external validation)	DL	Yes

Table 3. *Performance of studies for classification.*

Study	# of patients	Cancer type	Radiopharma-ceutical	Classes	# of models	AUC of the model with the best results	AI sub-set	Radiomics utilization
Moazemi et al. [65]	72	Prostate cancer	^{68}Ga-PSMA	localized and metastasized prostate cancer	5	0.98	ML	Yes
Erle et al. [66]	72	Prostate cancer	^{68}Ga-PSMA	malignant and physiological findings	3	0.95	ML	Yes
Leung et al. [67]	214	Prostate cancer	^{18}F-DCFPyL	benign and malignant findings	1	0.90	DL	Yes
Zang et al. [68]	123	Prostate cancer	^{68}Ga-PSMA	prostate cancer and benign prostate disease	1	0.85	ML	Yes

Diagnosis

Artificial intelligence is capable of combining data from various sources to create an integrated diagnosis [69]. According to the study of Tong et al. (2022) when combined with clinical traits from non-small cell lung cancer (NSCLC) patients, PET/CT radiomics data can been used to evaluate tumor immune microenvironment (TIME) profiles [70]. For the purpose of analyzing TIME profiles in NSCLC, radiomics models (PET/CT, PET, and CT radiomics models) need to be created. Then, a multivariate logistic regression model (combined model) is constructed using the Rad-score and clinical features, and eventually, a predictive nomogram has to be developed to create a risk-scoring model. Using calibration curves, the nomogram's calibration is evaluated. The receiver operating characteristic (ROC) curve can be used to assess how well the models perform as diagnostic tools for predicting TIME profiles of NSCLC [70]. The results showed that the combined model performed better, than both the clinical model and the radiomics model in terms of accurately predicting TIME status in NSCLC [70].

Yan et al. (2020) developed a diagnostic model for histological subtypes in lung cancer by combining CT and PET imaging data. The study used an ML approach on 445 patients. The outcomes to be predicted were primary, metastases, adenocarcinoma, and squamous cell carcinoma [70].

Disease-free survival prediction

The probability of successful cancer treatment significantly improves with early diagnosis and prognosis [71]. Artificial intelligence can be used for predicting disease-free survival of early-stage uterine cervical squamous cancer. At Liu et al. (2022) study, the ROI of images is independently defined by nuclear medicine doctors. Following manual segmentation, the PyRadiomics package [73] can be used to automatically determine the radiomic features from tumor ROI, including shape, intensity, and texture [74].

At this study, the training set undergoes the three steps below for the selection of radiomic features. In order to assess the prognostic potential of each feature individually, the concordance index (C-index) can be used. A low C-index denotes a feature's poor prognostic predictive power. Low-C-index features should be eliminated. The variance inflation factor (VIF) can be used to quantify feature collinearity and eliminate redundancy from large number of features [75]. The feature with the highest VIF score ought to be eliminated after each iteration. Third, a multivariate analysis using the random survival forest (RSF) model is possible [74].

Strong discrimination was produced by the PET/CT radiomic model compared to the clinicopathologic model (0.9125 for the training set and 0.9019 for the testing set), with C-index values of 0.9557 for the training set and 0.9338 for the testing set. A comprehensive model was further developed by combining the radiomic and clinicopathologic features, and it achieved C-index values of 0.9717 and 0.9527 for the training and testing sets, respectively [74].

In another study (Ferreira et al. (2021)), one hundred fifty-eight patients with locally advanced cervical cancer (LACC) from multiple centers were retrospectively included. Tumor segmentation was performed using the fuzzy local adaptive bayesian (FLAB) algorithm. Radiomic features were extracted from the tumors and from regions drawn over the normal liver from PET images of cervical cancer and evaluated the performance of different classifiers together with different feature selection (FS) methods. As a result, we obtain an AUC of 0.56 for the best tumor-to-liver ratio (TLR) model [76].

Table 4. *Performance of studies for diagnosis.*

Study	# of patients	Cancer type	Radiopharmaceutical	# of models	AUC of the model with the best results	AI subset	Radiomics utilization
Tong et al. [70].	221	Lung Cancer	^{18}F-FDG	3	0.920	ML	Yes
Yan et al. [71].	445	Lung cancer	^{18}F-FDG	1	0.90 (for CT-based radiomics) 0.95 (for PET-based radiomics)	ML	Yes

Table 5. *Performance of studies for disease-free survival prediction.*

Model with the best results	# of patients	Cancer type	Radiopharmaceutical	AUC of the model	AI subset	Radiomics utilization
Liu et al. [74].	201	Cervical cancer	^{18}F-FDG	0.9527 (for combined model)	ML	Yes
Ferreira et al. [76].	158	Cervical cancer	^{18}F-FDG	0.56	ML	Yes

Treatment response

Another study (Moazemi et al. (2021)) aimed to use a ML method to investigate the role of radiomic signatures in PSMA-PET/CT scans and clinical parameters to predict response to lutetium-177-prostate-specific membrane antigen (^{177}Lu-PSMA) treatment. The AUC for the task of predicting treatment response was 0.8 [77].

Expanding on the significance of radiomic features, a noteworthy case highlighting their utilization in treatment decision making comes from the development of a PET/CT-based DL model in a prior study (Mu et al. (2020)). This model represents an additional advancement in treatment response prediction. This model was capable of accurately classifying the presence of EGFR mutations by integrating radiomics features [78]. A test cohort was employed in order to assess the effectiveness of the EGFR prediction model [78].

Discussion

The diagnosis and treatment of cancer patients could be greatly improved by incorporating AI into PET/CT imaging. AI methods can improve several PET/CT imaging processes, including image acquisition, quality evaluation, post-processing, and clinical decision support. AI algorithms can help PET/CT imaging become more accurate, effective, and capable of offering useful insights into tumor characteristics and treatment responses.

In the article, an overview of the bibliography was conducted in order to examine how AI has been used in PET/CT. This process resulted in the final collection of 12 articles (8 original research articles and 4 studies from one review article). It is discussed how AI is being used for segmentation, classification, diagnosis, disease-free survival prediction and treatment response prediction using PET/CT images for diverse types of cancer.

It appears that DFCN is a viable method for enhancing tumor segmentation accuracy in research and clinical settings, especially when using both PET and CT data. In addition to this, a DeepMTS model for tumor segmentation in ^{18}F-FDG PET/CT images demonstrates its effectiveness for automating tumor segmentation.

For the purpose of better lesion classification in patients, ExtraTrees can be an accurate classifier. The findings show that radiomics and machine learning have the potential to improve cancer lesion classification.

Artificial intelligence is also significantly enhancing healthcare in the field of cancer diagnosis. Moreover, the high AUC of the Random Forest model based on the top predictive features indicates its potential as a valuable tool to advance prostate cancer diagnosis by identifying previously overlooked tumor tissue.

Combining radiomic and clinical data increases predictive accuracy. Concurrently, the FLAB algorithm contributes to the prediction of disease-free survival through the utilization of radiomic features.

The analysis indicates that the application of AI in the domains of classification and diagnosis provides reliable results. Additionally, the majority of these studies employ ML techniques instead of DL. Also, radiomics utilization is observed in most of these studies.

Combining radiomic features from multiple imaging modalities enhances predictive models for treatment response. These findings demonstrate the multimodality approaches' superior performance. Simultaneously, the application of a ML method utilizing radiomic signatures from PET/CT scans, in combination with clinical parameters, demonstrates promising predictive capabilities for treatment response.

Another observation that emerges from these studies is the predominant utilization of image-based data as opposed to clinical data. The preponderance of the research works examined in this overview is centered on image-based information, highlighting a notable emphasis on visual diagnostic modalities.

The findings of this study highlight the significance of AI in improving cancer management by providing clinicians with useful tools to improve early diagnosis, forecast patient outcomes, and offer individualized treatment plans. As these technologies continue to evolve, there is a great chance that they will be widely used in clinical practice.

Although the results of applying AI to PET/CT imaging have been encouraging, there are still many problems to be fixed and actions to be taken. Integrating AI into clinical practice has difficulties. A large number of features for each in-

Table 6. *Performance of studies for treatment response prediction.*

Study	# of patients	Cancer type	Radiopharmaceutical	Assessment measures	AI subset	Radiomics utilization
Moazemi et al. [77]	83	Prostate cancer	^{177}Lu-PSMA	AUC = 0.8	ML	Yes
Mu et al. [78]	73	Lung cancer	^{18}F-FDG	AUC = 0.86(for training) AUC= 0.83(for internal validation) AUC= 0.81(for external validation)	DL	Yes

stance in the dataset must be handled in many machine learning applications. Working with a large number of features may present some challenges because of the slower training and increased risk of overfitting. Overfitting is a modeling error where a machine learning algorithm learns the training data too well, capturing noise and specific patterns that do not generalize well to new, unseen data. The test set performances being significantly worse than the training set performances is a sign of overfitting. In most cases, overfitting results from a model that is too complex for the underlying data [79].

Large and diverse datasets, as well as thorough validation and standardization, are necessary for the development of reliable AI models [80]. To demonstrate that AI algorithms are reliable and generalizable, rigorous validation methodologies must be orchestrated. In general, standardization is beneficial because it can increase the effectiveness, efficacy, safety, compatibility, and cost-effectiveness of goods and services [80]. To make sure that AI systems are deployed in healthcare settings safely and responsibly, ethical issues and data privacy concerns must all be carefully considered. Ethical concerns are of great importance in the context of AI integration [81].

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