Applications of Artificial Intelligence in PSMA PET/CT for Prostate Cancer Imaging

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Applications of Artificial Intelligence in PSMA PET/CT for Prostate Cancer Imaging

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Prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) has emerged as an important imaging technique for prostate cancer. The use of PSMA PET/CT is rapidly increasing, while the number of nuclear medicine physicians and radiologists to interpret these scans is limited. Additionally, there is variability in interpretation among readers. Artificial intelligence techniques, including traditional machine learning and deep learning algorithms, are being used to address these challenges and provide additional insights from the images. The aim of this scoping review was to summarize the available research on the development and applications of AI in PSMA PET/CT for prostate cancer imaging. A systematic literature search was performed in PubMed, Embase and Cinahl according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A total of 26 publications were included in the synthesis. The included studies focus on different aspects of artificial intelligence in PSMA PET/CT, including detection of primary tumor, local recurrence and metastatic lesions, lesion classification, tumor quantification and prediction/prognostication. Several studies show similar performances of artificial intelligence algorithms compared to human interpretation. Few artificial intelligence tools are approved for use in clinical practice. Major limitations include the lack of external validation and prospective design. Demonstrating the clinical impact and utility of artificial intelligence tools is crucial for their adoption in healthcare settings. To take the next step towards a clinically valuable artificial intelligence tool that provides quantitative data, independent validation studies are needed across institutions and equipment to ensure robustness.

Introduction

Prostate cancer is the second most common malignancy in terms of prevalence and the sixth leading cause of cancer-related death among men globally.[1] The disease stage at diagnosis highly influences treatment planning and prognosis.[2] In advanced prostate cancer, measuring changes in tumor burden over time is crucial to help guide therapy and

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to evaluate treatment effect. As there are no blood-borne markers to accurately reflect the disease spread, this task heavily relies on imaging.

Prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) has become increasingly important in recent years in prostate cancer imaging. PSMA is a type II transmembrane protein that is expressed in the epithelium of the prostate,[3] but also in for example proximal renal tubules and salivary glands.[4, 5] It is over-expressed in prostate cancer but also in several other cancer types.[5] PSMA expression increases with increasing prostate cancer stage and tumor grade.[6-8] PSMA ligands used for PET/CT imaging bind to the surface receptor and are internalized within the cells. Several PSMA ligands labelled with either gallium-68 (^{68}Ga) or fluorine-18 (^{18}F) exist with slightly different properties. Examples include [^{68}Ga]Ga-PSMA-HBED-CC ([^{68}Ga]Ga-PSMA-11), [^{68}Ga]Ga-PSMA-617, [^{68}Ga]Ga-PSMA-I&T, [^{18}F]DCFBC, [^{18}F]DCFPyL and [^{18}F]PSMA-1007. [^{68}Ga]Ga-PSMA-11 was introduced in humans in 2012 and is the most studied PSMA ligand and has been investigated in different stages of prostate cancer.[9-11] [^{18}F]PSMA-1007 is mainly excreted through the hepatobiliary pathway (instead of the urinary route common for other PSMA ligands) which might be advantageous for finding sites of local recurrence close to the urinary bladder.[12-15] [^{68}Ga]Ga-PSMA-11 and [^{18}F]DCFPyL are approved by the US Food and Drug Administration (FDA). Using PSMA PET/CT for finding sites of biochemically recurrent prostate cancer is a widely accepted clinical indication in many parts of the world, since several studies have indicated superior detection compared with conventional imaging.[2] Evidence is growing that it also is useful for staging high-risk primary prostate cancer.[16-19] It can also be used to determine eligibility for radioligand therapy using for example [^{177}Lu]Lu-PSMA-617, and possibly to monitor treatment effect in advanced prostate cancer.[20-23]

Considering all possible applications of PSMA PET/CT in a cancer type that affects a large part of the male population, it is easy to imagine that the number of PSMA PET/CT scans will increase faster than the working force of nuclear medicine physicians and radiologists. A problem of inter-reader variability also exists. Furthermore, the images may carry valuable information that is not known or clinically used today, such as predictive information. Artificial intelligence (AI) could be a part of the solution to these issues. The aim of this scoping review was to perform a systematic literature search of available research on development and applications of AI in PSMA PET/CT for prostate cancer and to summarize the results.

Artificial Intelligence

The aim of AI is to replicate and even exceed human cognitive capabilities in various domains, including image analysis. Within image analysis, AI includes tasks such as:

- Image classification, ie, assigning a label or a category to an entire image,
- Object detection, ie, identifying and localizing of a set of objects in an image, and
- Semantic segmentation, ie, partitioning an image into multiple regions by assigning a class label to each pixel.

AI typically involves machine learning, which is a subfield that focuses on enabling computers to learn from data and make predictions or decisions without being explicitly programmed. For a long time, machine learning techniques such as support vector machines and random forests were popular in image analysis. However, these traditional machine learning methods can often struggle with the high dimensionality of raw pixel data and often rely on manually designed features to perform well. This limits their effectiveness in complex visual tasks and makes development a rather tedious process of manual fine-tuning and feature design.

Deep learning is a subfield of machine learning that deals with algorithms inspired by the structure and function of the brain, specifically neural networks with several layers. For image analysis, a special architecture called convolutional neural networks (CNNs) have proven to be especially useful. Like other deep learning models, CNNs can learn hierarchical feature representations directly from raw pixel data alleviating the need for manually designed features.

Although CNNs have been around for more than 30 years, their real breakthrough came about a decade ago, probably due to an increased availability of large datasets and more powerful computing hardware, including graphics processing units. Since then, CNNs and more recently vision transformers, have drastically improved state of the art for a wide range of image analysis tasks and sometimes coming close to or even surpassing human performance, particularly when large annotated datasets are available.

Radiomics is a group of methods closely related to classical machine learning as it involves the extraction of a large number of quantitative features from medical images, such as shape, texture, and intensity characteristics. Machine learning techniques are then employed to build predictive models using these radiomic features.

Methods

Literature Search and Screening

The literature search was performed in PubMed, Embase, and Cinahl between 17 to 21 March 2023. It was a combined search of AI (including machine learning, deep learning, neural networks, computer neural networks and conventional neural networks); prostate cancer; PSMA (including DCFPyL), and PET/CT. Limitations were set in languages (only English, Danish, Norwegian, and Swedish) and article type (editorials, letters, comments, notes, and erratum were excluded). Deduplication of the results was done in EndNote. For complete search strategies, see Supplement 1.

The literature search resulted in 199 hits. After deduplication, 160 unique articles remained. The articles were then

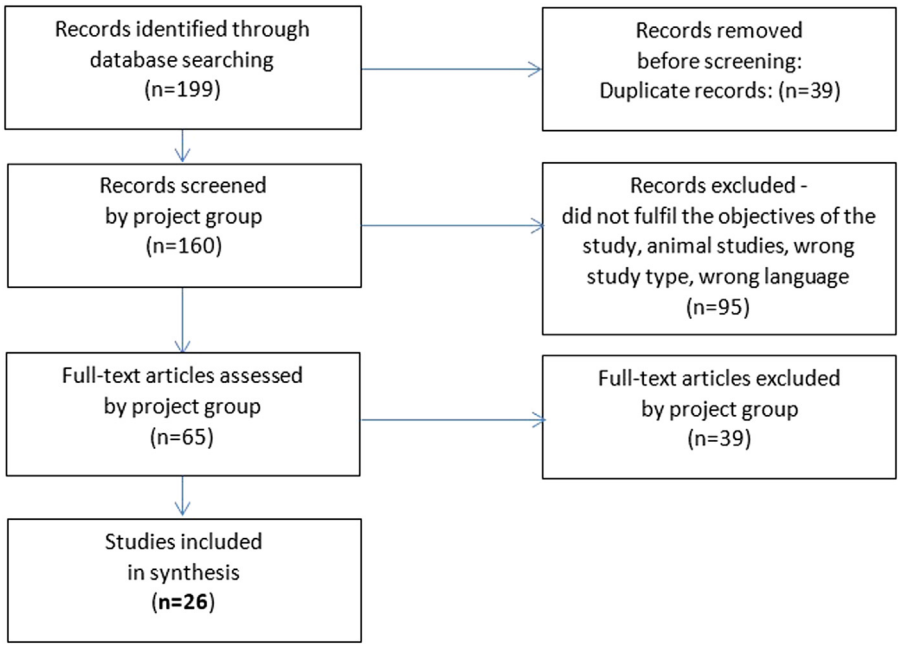

Figure 1 PRISMA flow chart.

screened in abstract independently by two researchers with the screening tool Rayyan. Conflicts were solved by consensus. Articles that did not fulfil the objectives of the study, animal studies and/or articles with the wrong article type or the wrong language were excluded. The remaining articles were assessed in full text, or in HTML-format if full text was unavailable. Only articles that fulfilled the objectives were included in the synthesis.

Sixty-five articles remained after screening. In the synthesis, 26 articles were included. For more information, see the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart (Fig. 1). An overview of all included original research papers are presented in Supplement 2.

Detection

Many publications present methods that apply AI for automated detection and segmentation of both primary tumor and metastatic lesions. This is intuitively appealing given the possible time-sparing profits, especially in patients with metastatic castration-resistant prostate cancer (mCRPC) with widespread disease. For prostatic lesions, AI-assisted segmentation can be used for radiomic features extraction or to improve treatment planning for focal radiation therapy.

Two articles were found that focus on detection of lesions in the pelvic region. Zhao et al.[24] developed a model using [^{68}Ga]Ga-PSMA-11 PET/CT scans from 193 patients with mCRPC from three different centers. A triple-combining 2.5D U-Net pipeline was trained using manual segmentations by two physicians. The cohort had a high burden of disease with a total of 1003 bone lesions, 626 lymph node lesions, and 127 local lesions in the pelvic region. When evaluated against the manual segmentations, the sensitivity for detection of both bone lesions (sensitivity 99%) and lymph nodes (sensitivity 90%) was high, but low for the detection of prostatic lesions (sensitivity 61%). The number of false positives was not stated. The model was subsequently tested on 35 [^{68}Ga]Ga-PSMA-11 PET/CT scans from a Chinese patient cohort with similar accuracy.[25] In a study by Trägårdh et al.[26] a CNN-based model for detection of pelvic lymph nodes in [^{18}F]PSMA PET/CT achieved a high sensitivity of 82%, compared to 77% for physicians. The average number of false positive lesions per patient was only 1.8. The study included 211 patients who had performed a [^{18}F]PSMA PET/CT scan as part of initial staging and did not limit the field of view to the pelvis, making it difficult to compare to the study by Zhao et al.

Other publications present CNN-based models for whole-body lesion detection. In a subsequent study, the model by Trägårdh et al.[27] was further developed to detect both prostatic lesions and metastases, and to quantify the whole-body tumor burden. The material was extended to 660 [^{18}F]PSMA-1007 PET/CT scans from patients with newly-diagnosed high-risk prostate cancer or with suspected recurrent disease after initial treatment. The model had an average sensitivity of 79% for the detection of primary tumor or local recurrence with physicians as reference (compared to an average sensitivity of 78% for physicians when compared to another reader), 79% for the detection of lymph node lesions (78% for physicians), and 62% for the detection of bone metastases (59% for physicians). Thus, the performance of the AI tool was comparable to human interpretation.

Kendrick et al.[28] developed a model using a self-configuring nnU-net framework for fully automated whole-body lesion segmentation in [^{68}Ga]Ga-PSMA-11 PET/CT from 193 patients with biochemical recurrent prostate cancer. Manual segmentations were used as ground truth. On a lesion-level, the model achieved a sensitivity of 73% and positive

predictive value of 88% with a low false positive prediction rate (1 per 4.3 scans). On a patient-level, the accuracy, sensitivity and positive predictive value were > 90%, respectively. The patients had a low burden of disease, and the authors advocate validation in patients with higher tumor burden.

Capobianco et al. developed CNN-based method to support image-based staging by using training information from both [^{68}Ga]Ga-PSMA-11 and [^{18}F]FDG PET/CT.[29] The rational was to pretrain on [^{18}F]FDG information, with fine-tuning on [^{68}Ga]Ga-PSMA-11 data, given the limited availability of the latter. The CNN showed an agreement of 81% with expert assessment for the identification of pelvic lymph node involvement (N1), 62% in metastasis (M) stage assignment and 77% for identification of any distant metastases (M0 vs M1).

In a radiomics study, Cysouw et al.[30] aimed to develop a machine learning-based model for detecting metastatic disease in preoperative [^{18}F]DCFPyL PET/CT. They included 76 patients with intermediate- to high-risk prostate cancer scheduled for radical prostatectomy. Radiomic features (intensity, morphology and texture features) were extracted from the delineated primary tumor. The resulting random forest algorithm achieved a good discriminatory performance in the detection of both lymph node and distant metastasis (AUC 0.86, $P < 0.01$, respectively). The authors conclude that the model could constitute a noninvasive determination of low-risk patients that can be spared from extended pelvic lymph node dissection but would require external validation.

In a conference abstract, Xu et al.[31] trained and evaluated two different CNN-based models (a fully CNN with a ResNet-101 backbone and a U-Net) using [^{18}F]DCFPyl PET/CT scans from 526 patients with metastatic prostate cancer. The sensitivity (44%, not stated for which model) when compared to manual delineation was considerably lower compared to other authors and only up to five lesions per scan were segmented. Interestingly, proximity to bladder and lesion intensity ($SUV_{max} > 5$) were found to be important factors for detectability.

The remaining publications in this category include three conference abstracts and one manuscript.

One of the conference abstracts presents an experimental CNN-based method for removal of physiological radiopharmaceutical activity in [^{18}F]DCFPyl PSMA PET/CT,[32] and one introduces a CNN-based model for urinary bladder segmentation in [^{18}F]DCFPyl PSMA PET/CT.[33] Neither of the models are trained to perform lesion detection but can rather be regarded facilitative presteps. The third conference submission presents preliminary results from a CNN-based model for detection of bone lesions in [^{68}Ga]Ga-PSMA PET/CT.[34] Finally, Ghezzo et al.[35] present a CNN-based model for segmentation of primary tumor in [^{68}Ga]Ga-PSMA PET/CT with a median Dice similarity coefficient of 0.77 compared to manual delineation.

Classification

Other publications focus on classification rather than detection of suspected metastases. Moazemi et al.[36] tested five different machine learning models for classification of 2419 lesions in 72 patients that had been treatment for either localized or metastasized prostate cancer and referred for a follow-up [^{68}Ga]Ga-PSMA PET/CT. Lesions were delineated by two physicians and a total of 80 features (40 from PET and 40 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. In a similar study, Erle et al.[37] compared three different machine learning radiomics models based on support vector machine, ExtraTrees and random forest models, respectively. The models were trained to differentiate between malignant and physiological uptake in [^{68}Ga]Ga-PSMA-11 images. A total of 2452 hotspots were delineated in 72 patients and marked either as malignant or physiological. A total of 77 radiomic features were utilized in each algorithm, with an ExtraTree classifier showing the best results (AUC 0.95, sensitivity 95%, and specificity 80%).

Leung et al. developed a radiomics model to perform patient-level and lesions-level classification in [^{18}F]DCFPyl PET scans from patients with prostate cancer (inclusion criteria or stage not stated).[38] Instead of using the maximum relevance and minimum redundancy method or similar to extract the most important features, a deep learning approach was used to automatically segment lesions and extract features.[38] A total of 3062 lesions from 214 patients were used for training and 53 patients with a total of 732 lesions were used to test the model (patient-level AUC 0.90).

Zang et al.[39] developed a radiomics model to differentiate between prostate cancer and benign prostate disease. They developed a radiomics model score constructed by a linear combination of coefficients from a selection of nine radiomic features and used a Least Absolute Shrinkage and Selection Operator (LASSO) algorithm to tune the parameters using a training set of 87 patients. The model was validated in a test set with 36 patients (AUC 0.85, sensitivity 84%, and specificity 77%).

Hartenstein et al. trained CNNs for the binary classification of lymph nodes in contrast-enhanced CT scans of 549 histologically confirmed prostate cancer patients (2616 segmented lymph nodes) using [^{68}Ga]Ga-PSMA-11 PET/CT as ground truth.[40] The model achieved an accuracy of 89% (AUC 0.95, sensitivity 86%, and specificity 92%) and performed comparable to physicians. However, histopathological confirmation was lacking and the author's state that the model lacks generalizability and relies on manual detection and segmentation of lymph nodes.

Prediction and Prognostication

Assessment of tumor burden could provide prognostic information and be used to evaluate treatment response.[41-44] To be clinically useful, tumor burden calculation needs to be fast and validated. In the study by Kendrick et al.[28] an additional evaluation of the CNN-based model was performed by

demonstrating that automated global biomarkers derived from [^{68}Ga]Ga-PSMA PET/CT were significantly associated with overall survival. Both total lesion volume (TLV) and total lesion uptake (TLU) were able to stratify patients based on the median values and a statistically significant difference in overall survival was seen in the two groups for both TLV and TLG ($P < 0.005$, respectively).

In the study from 2022 by Trägårdh et al, fully automated CNN-based calculation TLV and TLU obtained from prostate tumor/local recurrence, lymph node metastases, and bone metastases, showed a significant correlation to tumor burden estimation by physician's (range $P = 0.53$ [TLV lymph node metastases] to 0.83 [TLU prostate tumor/local recurrence]).[27]

In a conference abstract, McIntosh et al.[45] present a fully automated method for total tumor burden segmentation, developed using a CNN and a watershed filtering technique. The CNN was trained using 48 [^{68}Ga]Ga-PSMA PET/CT scans and tested in 50 patients and performed comparable to nuclear medicine physicians. The mean difference for $PSMA_{mean}$, $PSMA_{max}$, and $PSMA_{vol}$ derived from the total tumor burden segmentation was −0.2 SUV, −1.6 SUV and −153 mL with r 0.98, 0.97, and 0.93, respectively, when compared to the manual measures.

Other authors have focused on the possible predictive information contained in the primary tumor. Yi et al.[46] developed a machine learning-based radiomics model to predict undetected prostatic lesions on [^{68}Ga]Ga-PSMA-11 PET/CT. They manually segmented the prostate gland in 64 patients for training and 36 patients for testing the model. The ten most predictive features were selected, and a random forest model was used to predict the presence of undetected tumor tissue (AUC 0.93, sensitivity 85%, and specificity 88.5%). Yao et al.[47] used a support vector machine-based radiomics model on [^{18}F]PSMA-1007 PET scans to predict Gleason score, extracapsular extension, and vascular invasion, and evaluated how different thresholds of the segmentation process affect the prediction accuracy. Bezzi et al.[48] and Feliciani et al.[49] have in contribution to conferences described [^{68}Ga]Ga-PSMA-11 machine learning-based radiomics models to predict International Society of Urological Pathology (ISUP) score in patients with primary prostate cancer.

Evaluation for [^{177}Lu]Lu-PSMA-617 Therapy and Dosimetry

[^{177}Lu]Lu-PSMA-617 is an intravenous radioligand therapy combining a PSMA-targeting agent with the therapeutic radionuclide lutetium-177 (^{177}Lu). It has been reported to improve both progression-free survival and overall survival in patients with advanced prostate cancer who do not respond to any other available treatment.[20] In 2022, [^{177}Lu]Lu-PSMA-617 therapy for patients with PSMA-positive mCRPC who have received androgen receptor pathway inhibition and taxane-based chemotherapy was approved by both the FDA and the European Commission. As a theranostics approach, a pretreatment PET/CT scan using PSMA-targeting radiopharmaceuticals is routinely performed. Despite confirmed PSMA positivity, up to 1 of 3 of patients receiving [^{177}Lu]Lu-PSMA-617 therapy progress during treatment.[50] Strategies to discriminate responders from non-responders are therefore needed. Moazemi et al.[51] developed a method for treatment response prediction in 83 patients undergoing [^{177}Lu]Lu-PSMA-617 therapy based on baseline [^{68}Ga]Ga-PSMA PET/CT using a machine learning approach, with an AUC of 0.80 and a sensitivity and specificity of 75%, respectively.

Another challenge in [^{177}Lu]Lu-PSMA-617 treatment planning is to estimate the absorbed radiation dose in advance of therapy. In current practice, all patients are usually administered a fixed activity without individualized dose application. This opposes the European Commission directive which mandates the use of dosimetry-based treatment planning and verification for radiopharmaceutical therapies.[52] AI has been applied to bridge the gap to dosimetry-guided [^{177}Lu]Lu-PSMA-617 treatment planning. Xue et al.[53] used features from pretreatment [^{68}Ga]Ga-PSMA PET/CT and blood tests as input to train a traditional machine learning technique (random forest) and an artificial neural network. Both models showed a more accurate performance than population-based dosimetry on dose prediction for target organs.

Available Tools for Research or Clinical Use

If AI-based methods are to be incorporated into clinical routine, and thereby add benefit in the clinical work-up, validated and approved products are necessary. To date, only one product for automated image analysis of PSMA PET/CT is approved by regulatory authorities. aPROMISE is CE-marked and FDA-cleared since 2021. The software offers quantitative analysis of hotspots and standardized reporting of PSMA PET/CT scans (Fig. 2). aPROMISE was trained to segment organs of low-dose CT based on a U-net architecture and [^{18}F]DCFPyL PET/CT scans were used for hotspot detection, based on classical blob detection within the relevant organ or region mask. In a retrospective study, the sensitivity for detecting suspicious metastases was found to be high, ranging between 87% (for bone) and 92% (for regional lymph nodes) depending on study cohort using the manually selected lesions as reference method.[54] However, the number of false positive lesions per patient was rather high, ranging from eight instances per patient for bone lesions and 90 instances per patient for lymph node lesions. In another retrospective setting, a high inter-reader agreement (Cohen pairwise kappa agreement of 0.77-0.90 for different stages) was found when using aPROMISE assisted reading.[55] The readers were able to accept or override the lesions suggested by the software. No information regarding the need for manual corrections was provided in the article. The reading time, from selecting a patient to generating a report, ranged from 2 to 6 minutes per patient. It is not known how the software

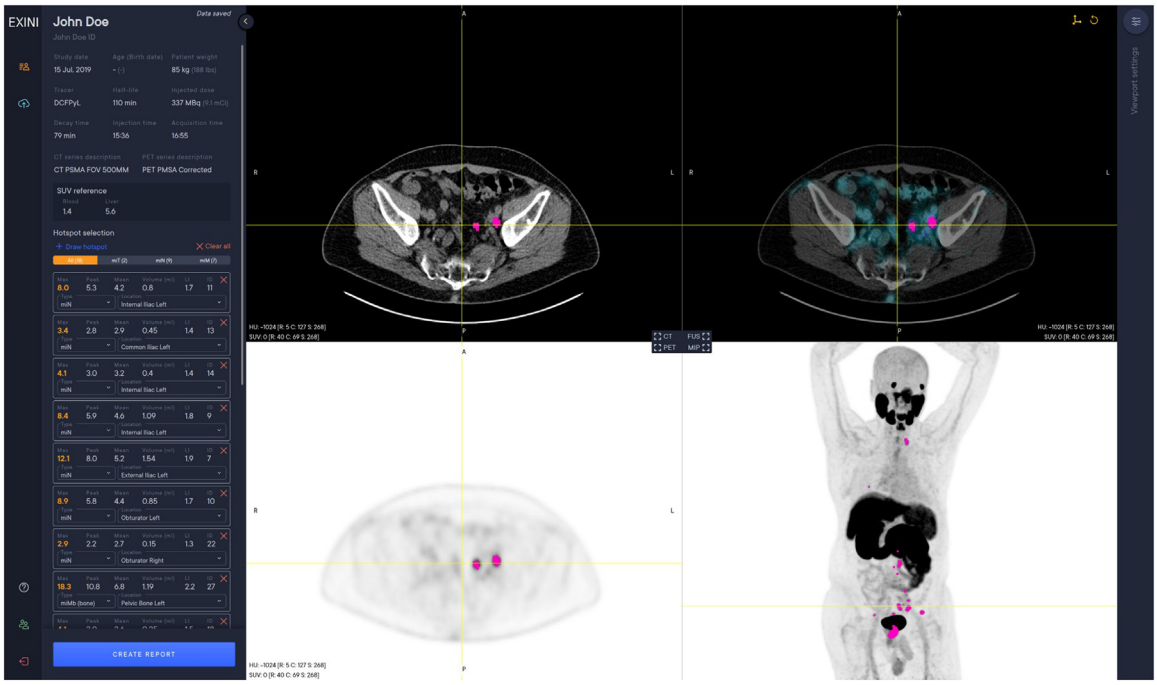

Figure 2 aPROMISE is the only CE-marked and FDA-cleared AI tool for analysis of PSMA PET/CT. It is based on a machine-learning model to detect high local intensity regions of interest (pink) in the PET series. The hotspots selected by the user are automatically quantified as shown in the table to the left.

works on other PSMA radiopharmaceuticals or if a diagnostic CT with intravenous contrast is used.

Two other authors have made their AI tools freely available to other researchers in order to promote independent validation. The tool used in the studies by Trägårdh et al.[26,27] is available at https://www.recomia.org (Fig. 3). The CNN-model by Ghezzo et al. for automatic segmentation of prostatic lesions in [^{68}Ga]Ga-PSMA PET/CT is available at

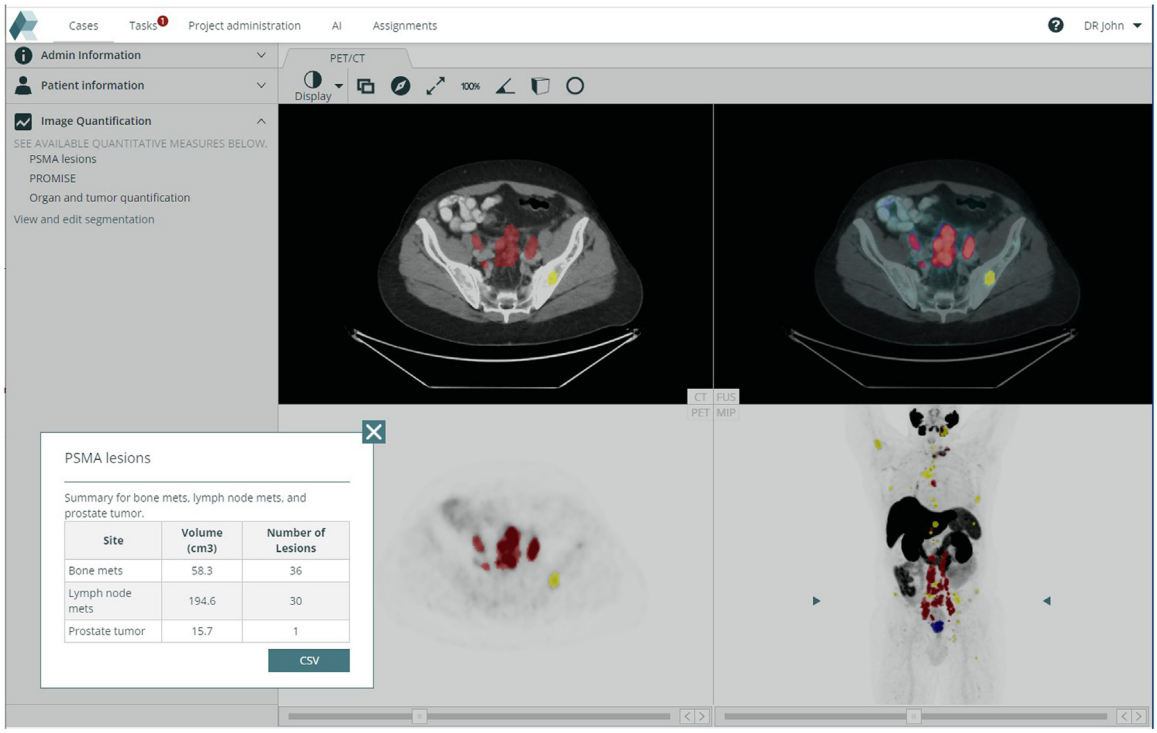

Figure 3 The not-for-profit organization RECOMIA invites researchers to apply the artificial intelligence tool for PSMA PET/CT on their own PET/CT studies. The tool detects and quantifies prostate tumor (blue), lymph node lesions (red), and bone lesions (yellow).

https://gitlab.com/dejankostyszyn/prostate-gtv-segmentation.[35]

Discussion and Future Applications

In this scoping review, we have found several research projects that develop AI algorithms for PSMA PET/CT in prostate cancer. Research groups have worked on different aspects, such as lesion detection, lesion classification, quantification of tumors and prediction/prognostication. One CE- and FDA-approved product was found, trained on [^{18}F]DCFPyL PET/CT scans. Some of the other studies have made their code or AI tools freely available for other researchers.

PSMA PET/CT is increasingly used in a time when radiologists and nuclear medicine physicians are faced with a high and increasing workload. Time to learn how to distinguish normal and abnormal patterns of the relatively new PSMA tracers is often limited for inexperienced readers. At the same time, the emergence of precision medicine comes with the need for quantitative data, ie, imaging biomarkers. The common qualitative way to report PET/CT studies will not be sufficient and manual segmentation of tumors is a very time-consuming task. In this context, AI tools will play an important role in supporting radiologists and nuclear medicine physicians to improve interpretation accuracy, decrease inter-reader variability, save reporting time, and to provide clinicians with quantitative data.

Several AI tools have been presented and the results show the feasibility of developing a tool for clinical use. The study of Trägårdh et al.[26] showed sensitivity on par with human readers at a reasonable level of false positive detection and also illustrated the well-known problem with inter-reader variability. AI tools have the potential to harmonize interpretations and quantifications of PET/CT studies.

To take the next step towards a clinically valuable AI tool that provides quantitative data, independent validation studies are needed. Most models in this literature search have been trained and tested with data from a specific site, where images have been collected in a specific way regarding camera system, amount and type of radiopharmaceutical given, acquisition time and accumulation time between administration of activity and scan time. These parameters affect image noise, contrast and resolution and the activity distribution in the patient.[15,56-59] All these variables affect the generalizability of the models. Also, the CE-marked and FDA-cleared AI tools for PSMA PET/CT studies aPROMISE (also marketed as PYLARIFY AI) have not been independently validated.[54,55] These issues need to be handled before use of AI can be generally clinically valuable, which in part can be addressed by for example following the EARL harmonization for imaging or using the ComBat harmonization of imaging biomarkers.[60,61]

An example of how to establish a clinically valuable imaging biomarker is the validation process of the Bone Scan Index. Preanalytic and analytic validation studies followed by a clinical validation based on data from a large phase 3 study was performed to qualify the Bone Scan Index as a clinically valuable imaging biomarker.[62-64] A similar process would be of great value for AI tools in PSMA PET/CT.

Conclusion

The use of AI techniques shows promise in addressing the challenges associated with the analysis and interpretation of PSMA PET/CT in prostate cancer. The performance of several AI models is equivalent to that of experienced nuclear medicine physicians. However, there are limitations that need to be addressed for the widespread adoption of AI tools in clinical practice. These limitations include the lack of external validation and prospective design in most of the reviewed studies. To ensure the robustness of AI tools, independent validation studies and trials assessing the real-world impact on patient outcomes are needed. Overcoming these obstacles requires collaboration among researchers, healthcare providers and regulatory bodies. Demonstrating the clinical utility and impact of AI tools is crucial for their integration into healthcare setting and for improving patient care.

Declaration of Competing Interest

OE is a board member and stockholder of Eigenvision AB, which is a company working with research and development in automated image analysis, computer vision, and machine learning. The other authors do not have any competing interests to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.semnuclmed.2023.06.001.

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