BJR

https://doi.org/10.1259/bjr.20210563

Received: 09 May 2021 | Revised: 26 October 2021 | Accepted: 17 November 2021

Cite this article as:
Turkbey B, Haider MA. Deep learning-based artificial intelligence applications in prostate MRI: brief summary. *Br J Radiol* 2022; **95**: 20210563.

INNOVATIONS IN PROSTATE CANCER SPECIAL FEATURE : REVIEW ARTICLE

Deep learning-based artificial intelligence applications in prostate MRI: brief summary

[1]BARIS TURKBEY and [2,3,4]MASOOM A. HAIDER

[1]Molecular Imaging Branch, NCI, NIH, Bethesda, MD, USA
[2]Lunenfeld-Tanenbaum Research Institute, Sinai Health System, Toronto, Ontorio, Canada
[3]Joint Department of Medical Imaging, University Health Network, Sinai Health System and University of Toronto, Toronto, Ontorio, Canada
[4]Ontario Institute for Cancer Research, Toronto, Ontorio, Canada

Address correspondence to: Dr Baris Turkbey
E-mail: *turkbeyi@mail.nih.gov*

ABSTRACT

Prostate cancer (PCa) is the most common cancer type in males in the Western World. MRI has an established role in diagnosis of PCa through guiding biopsies. Due to multistep complex nature of the MRI-guided PCa diagnosis pathway, diagnostic performance has a big variation. Developing artificial intelligence (AI) models using machine learning, particularly deep learning, has an expanding role in radiology. Specifically, for prostate MRI, several AI approaches have been defined in the literature for prostate segmentation, lesion detection and classification with the aim of improving diagnostic performance and interobserver agreement. In this review article, we summarize the use of radiology applications of AI in prostate MRI.

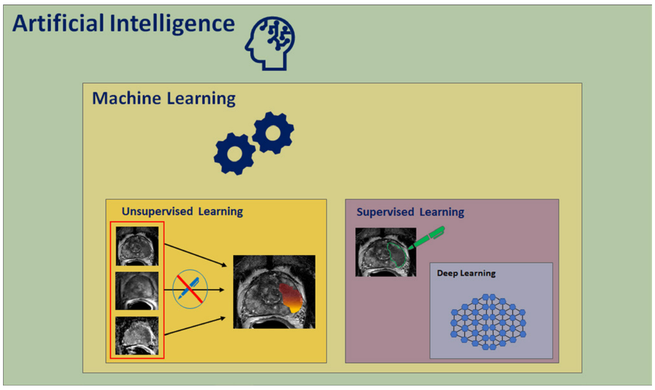
Prostate MRI has an established role in guiding prostate biopsies and diagnosis of clinically significant prostate cancers (PCas).[1–4] Although the benefit of use of MRI has been reported in studies mainly conducted in academic centers, it is evident that the diagnostic performance reported in large-scale academic studies cannot be widely reproduced.[5] Use of prostate MRI in diagnosis of PCa through the MRI-guided biopsy pathway has several key steps, such as MRI acquisition, interpretation/reporting, MRI data processing for biopsy use, and MRI to transrectal ultrasonography image registration during biopsy procedure, all of which make up a multistep quality chain.[6–8] In order to improve standardization of use of prostate MRI, the Prostate Imaging and Reporting Data System (PI-RADS) was developed and released by international experts in 2015[9] and currently its version 2.1 is in use.[10] Although PI-RADS has been documented to improve use of prostate MRI in PCa clinical care, its key elements are still subjective, which is prone to diminish robustness of prostate MRI, specifically in the community setting. Artificial intelligence (AI) has been shown to aid multiple tasks such as organ segmentation, lesion detection, classification in medical imaging including radiology and pathology.[11,12]

Machine learning (ML) is an important branch of AI and mainly serves as the basis for development and training algorithms for certain tasks which allows computers to learn from human expert-driven data and predict certain outcomes. ML algorithms can be stratified in three categories:

(1) Supervised learning: Algorithm training is dependent on a ground truth training data labeled by human experts.
(2) Unsupervised learning: Algorithm training is independent of training data labeled by human experts.
(3) Reinforcement learning: Algorithm training is adaptive and is based on continuous feedback from its own mistakes and successes.

ML strategy can analyze and recruit big-scaled data for training AI models which is much more efficient compared to traditional statistical approaches, and therefore it has an expanding role in radiology, where massive amount of data is produced continuously. Deep learning (DL) is a subset of supervised ML which employs algorithms also called convolutional neural networks (CNNs) with hidden layers in a structured fashion mimicking human neuron architecture. For radiology applications, traditionally imaging

Figure 1. Artificial intelligence development methods currently in use.



data are transformed into integrated feature vectors which build the input neurons of the network, and this is followed by a number of hidden layers made up by neural nodes. Each node is then connected to those in other layers with different weights, which determine the strength of connections between neurons, leading to the output neurons that encode the model outcome (Figure 1).[13] In the last half decade, there has been a growing interest in use of DL-based AI applications in prostate MRI[14,15] and in this review article, we will summarize use of radiology applications of AI in prostate MRI.

AI IN PROSTATE MRI SCAN QUALITY

As prostate MRI has been more widely used, this has led a large variation in scan quality. Scan quality is closely related to factors, such as equipment used, pulse sequence parameters and patient-related factors (*e.g.* hip prosthesis, motion, and rectal gas). The PI-RADS v. 2.1 document provides minimum technical specifications and patient preparation options to improve quality of prostate MRI.[10] The adherence to PI-RADS technical standards is quite variable,[16,17] and stringent adherence to these technical standards do not necessarily ensure good quality prostate MRI scans.[18] Additionally, the actual impact of patient preparation measures, such as bowel preparation or use of antispasmodic agents, is quite variable.[19–22] Several groups in the world are exploring routes of improving prostate MRI quality and, recently, Prostate Imaging quality (PI-QUAL) has been released by European prostate MRI experts.[23] This system aims to evaluate the diagnostic quality of prostate MRIs using a set of criteria for each pulse sequence.[23] PI-QUAL has been recently investigated in an interreader agreement study with 103 patients and 2 dedicated radiologists. The agreement for each single PI-QUAL score was strong ($\kappa = 0.85$ and percent agreement = 84%). The agreement for diagnostic quality of each pulse sequence was 89% (92/103 scans), 88% (91/103 scans) and 78% (80/103 scans) for T_2 weighted imaging, dynamic contrast-enhanced MRI and diffusion-weighted imaging, respectively.[24]The actual impact of PI-QUAL evaluation system on improving prostate MRI quality will soon be reported. Use of AI in evaluation and improving prostate MRI scan quality is an understudied topic and very few studies exist. In a pilot study with 30 patients, Gassenmaier et al utilized a novel DL T_2 weighted turbo spin echo imaging (T_2DL) sequence in prostate MRI and investigate its impact on examination time, image quality, diagnostic confidence, and PI-RADS classification compared to standard T_2 weighted turbo spin echo imaging. The DL algorithm in that study relied on data consistency through a parallel imaging signal model and was trained on a pool of representative data which resulted in more suited regularization allowing faster image acquisitions. The fixed unrolled algorithm for accelerated MR image reconstruction consisted of multiple cascades, each made up from a data consistency using a trainable Nesterov momentum followed by CNN-based regularization. The regularization model's architecture was based on a novel hierarchical design of an iterative network that repeatedly decreases and increases the resolution of the feature maps, allowing for a more memory-efficient model than conventional CNNs. As input to the network, undersampled k-space data and conventionally estimated coil-sensitivity maps were provided. The DL-based T2 sequence image acquisition was shorter than the standard T2 sequence (1:38 min *vs* 4:37 min). Noise level was lower, and image quality was rated higher for the DL-based T2 sequence, which resulted in a better lesion detection performance.[25] This feasibility study needs further validation is larger cohorts.

It is quite evident that radiologists can perform much better if good quality imaging studies can be consistently provided to them during their read-outs. For prostate MRI, several initiatives exist for improving quality and use of AI for this purpose is currently in its infancy. However, implementation of AI-based MRI quality models into structured systems, such as PI-QUAL, can further improve this process.

AI IN PROSTATE GLAND SEGMENTATION

Planimetric delineation (also known as segmentation) of the prostate at MRI has critical clinical uses, such as accurate estimation of the entire prostate gland volume for normalizing the serum prostate-specific antigen (PSA) density as suggested by PI-RADS v. 2.1 and MRI data preparation for biopsy guidance in transrectal ultrasonography/MRI fusion-guided biopsy systems and for radiotherapy planning.[26] Manual delineation of the prostate is often time-consuming and prone to human errors.[27] AI has been commonly used for prostate segmentation and currently, there are few commercial solutions for this time-consuming task of prostate MRI data processing.[28] Recently, DL-based AI solutions are reported commonly to provide robust performance for segmenting prostate gland and its zones. In a study by Wang et al, a three-dimensional (3D) fully convolutional network with deep supervision was used to develop a fully automated prostate segmentation model for T_2 weighted MRI. The authors reported a mean dice similarity coefficient (DSC) of 0.88 (range, 0.83–0.93) between AI model and manual segmentations for the whole prostate.[29] In another study with 299 MRI studies, Ushinsky et al developed a hybrid 3D–2D U-net-based segmentation algorithm for automatic localization and segmentation of prostate gland at T_2 weighted MRI. The AI-based whole prostate segmentation model achieved a mean DSC of 0.898 (range, 0.890–0.908) when compared with manual segmentations.[30] Finally, in a study by Sanford et al, which included 648 patients, a DL approach combining 2D and 3D architectures with transfer learning incorporation was used to develop a whole prostate and transition zone (TZ) segmentation algorithm. The study reported mean DSCs of 0.931 and 0.89 for whole prostate and TZ, respectively. This study utilized a data augmentation strategy which was specific to the deformations, intensity, and alterations in image quality seen on MRI data from five different centers, and this novel strategy improved the whole prostate and TZ segmentation performances 2.2 and 3%, respectively.[31] In a recent study by Bardis et al with 242 patients, a DL model based on three convolutional networks with a U-net architecture had mean DSCs of 0.94, 0.91 and 0.774 for whole prostate, TZ and PZ, respectively.[32]

Prostate segmentation is the most commonly studied application with AI among others for prostate MRI. Although several algorithms exist in the literature, five prostate segmentation AI algorithms exist in commercial platforms for users. All of these tools are approved for use in USA by FDA [Prostate MR® (Siemens), Quantib Prostate® (Quantib), OnQ Prostate® (Cortechs.ai), PROView® (GE Medical Systems), qp-Prostate® (Quibim)], whereas two are approved in Europe [Prostate MR® (Siemens), Quantib Prostate® (Quantib)].[33,34] Having robust AI algorithms for prostate segmentations can certainly diminish the time needed for preparing MRI data for biopsy purposes and it can enable accurate calculation for PSA density for better risk stratification. Additionally, automated segmentation of the prostate and its zones can further boost performance of intraprostatic lesion detection and classification algorithms.

AI IN INTRAPROSTATIC LESION DETECTION

Intraprostatic lesion detection is the most critical step of reading prostate MRI, as this directly impacts performance of clinically significant PCa detection using MRI guidance. Considering the wider use of prostate MRI in community setting, a robustly working AI system with a balanced true-positive *vs* false-positive rate is almost always desired. In a 335-patient study, Ishioka et al developed a DL-based model which utilized U-net and ResNET architectures for detecting targeted biopsy-confirmed PCa lesions. They evaluated their model in two separate populations and the model had an area under the curve (AUC) of 0.636 and 0.645 for PCa detection.[35] Schleb et al developed and tested a U-net-based DL model, which was trained in 250 patients for detection of targeted biopsy-confirmed cancer suspicious lesions at MRI. In the test set, PI-RADS cut-offs 3 and above *vs* 4 and above on a per-patient basis had sensitivity of 96% *vs* 88% and specificity of 22% *vs* 50%.[36] In another study by Arif et al with 292 low-risk PCa patients, a U-net-based DL model achieved an average sensitivity of 82–92% with an AUC of 0.65–0.89 for detecting targeted biopsy-confirmed PCa lesions with volumes ranging from >0.03 to >0.5 cc.[37] AI algorithms tend to perform better with larger data sets available for training. In a study by Yoo et al with 427 cases, who underwent MRI and guided biopsies, for a ResNet architecture-based neural network training, the reported AUCs for PCA detection in a separate 108 sample size test cohort were 0.87 and 0.84 at slice and patient level, respectively.[38]In a multireader study by Winkel et al, a DL-based AI system's impact on radiologists' interpretation accuracy and efficiency in reading biparametric prostate MRI was evaluated. The study included 100 open-source cases and 7 radiologists performed 2 rounds of read-out with and without AI using a 2-week washout period. The tested AI system was a commercial one which was approved in Europe and the United States. Use of AI system improved the average performance of radiologists from 0.84 to 0.88 for finding PI-RADS >3 lesions. Interreader agreement also increased from κ = 0.22 to 0.36; whereas the median reading time in the unaided/aided scenario was reduced by 21% from 103 to 81 s. This multireader study did not incorporate histopathology validation and aimed to mimic a pre-biopsy radiologist read-out scenario. Despite this limitation, it serves as a good study design example for proper evaluation of lesion detection AI systems for prostate MRI.[39] In a recent study by Saha et al, a multistage 3D AI model comprised two parallel 3D CNNs (dual-attention U-net detector and residual classifier) followed by a decision fusion node for automated detection of clinically significant PCa at biparametric MR imaging (bpMRI) was developed in 1950 patients and testing was conducted in 486 patients. The authors reported sensitivity values of 83.69 ± 5.22% and 93.19 ± 2.96% at 0.50 and 1.46 false positive(s) per patient, respectively, with 0.882 ± 0.030 area under the receiver operating characteristic in patient-based diagnosis which significantly outperformed four state-of-the-art baseline architectures (U-SEResNet, UNet++, nnU-Net, and Attention U-Net). Interestingly, this AI model had a reasonable agreement with expert radiologists (κ = 0.51±0.04) and pathologists (κ = 0.56±0.06).[40] AI is recently being more heavily investigated for PCa detection and a recent meta-analysis with 12 studies yielded an overall pooled AUC of 0.86, with 0.81–0.91 95% confidence intervals in clinically significant PCa identification.[41] Although the currently reported results are promising for AI applications in PCa detection with MRI, some limitations exist. First, DL-based AI algorithms naturally require large-scaled, diverse and well-annotated training and independent testing data sets. The current evidence in the literature is mostly based on studies with <1000 case sample sizes, and this most likely prevents wide applicability of the currently available AI systems. Construction of a large, multicenter and resultantly diverse data sets for developing stronger AI models can be challenging since data governance regulations can vary geographically and the bureaucracy can often be time and resource consuming. Alternate solutions for developing robust AI model without data sharing but with model sharing, such as federated learning, can be quite useful to enable accelerated development of models across institutions, enabling greater generalizability in clinical use without actual data sharing.[42] The currently reported performance metrics are mostly based on cross-validation and do not include an actual radiologist *vs* AI interaction, and these studies are far from representative of a real-world setting. Such an interaction and the implications of the mismatches between radiologist reads and AI outcomes are quite unknown. No doubt future research will yield the actual use and utility of AI in PCa detection at MRI. Finally, there are four commercially available platforms which include AI algorithms for PCa lesion detection and classification tasks, three of these tools are approved for use in Europe [Prostate MR® (Siemens), Quantib Prostate® (Quantib), JPC-01K® (JLK Inc.)], whereas three are approved by USFDA [Prostate MR® (Siemens), Quantib Prostate® (Quantib), PROView® (GE Medical Systems)].[33,34]

AI IN PI-RADS CLASSIFICATION AT MRI

PI-RADS classification is another critical component of prostate MRI read-out. PI-RADS employs a 5-tier category approach and as category number increases the likelihood of that particular lesion for including clinically significant PCa (>Gleason Grade 1) increases gradually (*e.g.* category 5 = very highly likely to include clinically significant PCa).[43] Lesion categorization is heavily based on subjective imaging features at T_2 weighted, diffusion-weighted and dynamic contrast-enhanced pulse sequences, which is often reported to have high interreader variation, which directly hampers wide use of prostate MRI.[44,45] Recently, very few studies report to use AI for PI-RADS categorization for intraprostatic lesions detected at MRI. Zhong et al used a ResNet-based CNN to detect and classify prostate lesions as indolent or clinically significant (equal or above PI-RADS 4). T_2W and apparent diffusion coefficient MR data of 110 patients were used to train this DL model. The model achieved an AUC of 0.73 for predicting lesions with a PI-RADS category of 4 and above.[46] In another study, Sanford et al developed an automated PI-RADS classification system using a CNN with ResNet 34 architecture. They used T_2W, diffusion-weighted MRI of 687 patients for AI development and compared AI's performance with an expert radiologist and assessed interreader agreement with an independent radiologist. The AI system was most successful at assigning the same PI-RADS score as the study radiologist on lesions that received PI-RADS scores 4 and 5 (~55 and 80% respectively, and much lower for PI-RADS scores 3 and 2). Since no statistically significant difference was found between AI's and radiologist's PI-RADS scores and histopathologic grade (Gleason grade), the overall conclusion was that AI is more consistent than the radiologist in correctly predicting high risk (PI-RADS 4 or 5) lesions and overall, the proposed AI system had similar agreement as between the study radiologist and an independent radiologist, with κ scores of 0.4 *vs* 0.34, respectively.[47]

Intraprostatic lesion PI-RADS classification is a relatively new topic in prostate imaging AI. Currently available AI algorithms report comparable results with expert-based PI-RADS read-outs and this can be quite helpful to aid non-dedicated body radiologists during their prostate MRI evaluations. However, the field remains constrained by the limited availability of well-curated diverse data.

EVOLVING REGULATORY LANDSCAPE AND OTHER USE CASES

For AI systems to be used in clinical practice, regulators must define a framework for approval. With organizations, such as the American Food and Drug Administration as of early 2021, this remains a work in progress. All software systems in use today involve use cases with some form of human supervision. Fully autonomous use cases for AI systems are not quite ready for prime-time and how these will be regulated remains unclear. Requirements for defining real-world performance of AI software systems remain a challenge given among a host of issues the potential for baked in biases in data used for training and testing. It is expected that the regulatory landscape will continue to evolve. Furthermore, transparency and full disclosure of methodology and training and testing data used to develop of AI tools approved, and we may use in our day-to-day practice has been generally lacking. Many of these issues and solicitation for community input have been recently expressed by the Food and Drug Administration.[48] Finally, there is great potential for super-human use cases where AI models can predict outcomes and help makes decision by analyzing large and deep data sets on individual patients that include a suite of lab results, comorbidities, genomics, family history etc. which is beyond our capacity as radiologists to synthesize. Appropriate data infrastructure to develop such models is an important step to see such super-human performance in the future.

CONCLUSION

In conclusion, prostate MRI is more commonly used in the last decade. Use of prostate MRI for PCa diagnosis is subject to several critical steps almost which are currently prone to human errors. AI in imaging has made great strides in the past few years and AI-based systems have been reported to perform tasks that are typically performed by diagnostic radiologists, such as scan quality evaluation, prostate segmentation, lesion detection and PI-RADS classification in research setting. While there are existing commercial AI platforms for prostate MRI, majority of the research-based AI solutions aiding these steps need training with larger-scaled, diverse data sets and the AI models need to be tested in real-life setting before a routine use in the clinical practice.

DISCLOSURE

Disclosures (Baris Turkbey):
1. "Project PI" CRADA: NVIDIA
2. CRADA (Research agreement): Philips
3. Royalties from NIH
4. Patents in the field of AI
Disclosures (Masoom Haider):
No disclosures

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