The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1557986

REVIEW

Artificial Intelligence in Prostate Cancer Diagnosis

Adem Alçın, Asıf Yıldırım
Department of Urology, Istanbul Medeniyet University, School of Medicine, Istanbul, Türkiye

Submitted: *2024-09-29*
Accepted: *2024-10-09*

Corresponding Author;
Adem Alcin, MD
Esenevler Neighborhood, Filizler Street, No:11/3 Umraniye/Istanbul, Türkiye
E-mail: alcinadem33@gmail.com

ORCID
A.A. 0000-0002-5026-5168
A.Y. 0000-0002-3386-971X

Abscract
Prostate cancer (PCa) is a cancer with a broad spectrum of biological behavior and it is a heterogeneous nature. In order to prevent overdiagnosis and overtreatment, and to detect clinically significant PCa, standardized scoring and grading systems are used in imaging and pathological examinations. However, reproducibility and agreement between readers in these diagnostic stages, which require experience, are low. Promising results have been achieved by integrating artificial intelligence (AI)-based applications into the diagnosis and management of PCa. In radiological and pathological imaging, computer-aided diagnostic tools have increased clinical efficiency and achieved diagnostic accuracy comparable to that of experienced healthcare professionals. This review provides an overview of AI applications used in radiological imaging, prostate biopsy, and histopathological examination in the diagnosis of PCa.

INTRODUCTION

Prostate cancer (PCa), the second most frequently diagnosed cancer in men, and it is definitively diagnosed through histopathological evaluation (1). Prostate sampling is performed via targeted and/or systematic biopsy under transrectal ultrasonography (TRUS) guidance to confirm cancer suspicion, which arises from elevated prostate-specific antigen (PSA) levels or suspicious digital rectal examination findings. With the use of standardized Prostate Imaging Reporting and Data System (PI-RADS) scoring through multiparametric magnetic resonance imaging (MpMRI) of the prostate prior to biopsy, MRI-targeted biopsies (MRI-TB) have been applied, gaining importance in diagnosing clinically significant PCa (csPCa) (2). The Gleason score is determined based on the histological features observed in tissue samples stained with hematoxylin and eosin (H&E), and grading is performed using the International Society of Urological Pathology (ISUP) grade grouping (3).

PCa has the widest biological behavior spectrum among urological cancers. It is mostly multifocal within the prostate gland, exhibiting a heterogeneous nature and a wide range of prognoses (4). The goal is to enhance diagnostic accuracy and csPCa detection rates while preventing unnecessary treatments and overdiagnosis. However, despite standardized pathological evaluation and supportive radiological imaging, there are some limitations. Interpreting MpMRI requires experience, and inter-radiologist agreement can vary (5). Due to the subjective nature of Gleason scoring and tumor heterogeneity, reproducibility between pathologists is

Cite; Alcin A, Yildirim A. Artificial Intelligence in Prostate Cancer Diagnosis. New J Urol. 2024;19(3):151-156. **doi:** https://doi.org/10.33719/nju1557986

poor (6). The use of artificial intelligence (AI)-based tools is increasing to improve clinical efficiency and diagnostic performance by reducing variability in interpretations among radiologists and pathologists (7).

Machine learning (ML) is an AI system that can automatically learn in an unsupervised manner or through supervised data labeled by humans by creating mathematical algorithms. Deep learning (DL) is a subset of ML that uses artificial neural networks to mimic the human brain and can independently derive nonlinear relationships and features (8). The ability of AI in diagnostic evaluation has brought its use in image analysis into the practice of pathology and radiology.

In this study, we present a summary of the use of AI in radiological and pathological evaluation for the diagnosis of PCa.

MpMRI Interpretation and Artificial Intelligence

Prostate MpMRI is recommended by guidelines for the local staging of PCa. Additionally, by combining MRI images and suspicious lesions with ultrasonography (US), fusion biopsy can be performed, contributing to increased diagnostic efficiency (9). AI applications in MpMRI have improved diagnostic performance by reducing the workload of radiologists in prostate segmentation, lesion detection, and characterization (10).

Despite the increased use of MpMRI and improvements in radiologist interpretation accuracy, particularly after standardization with PI-RADS, there are still some limitations. Meta-analyses have found the pooled specificity of MpMRI for PCa detection to be 0.73. It has been reported that 5-30% of cancers go undetected and readers have a 25% error margin (11,12). Another limitation is the low reproducibility of reporting among radiologists. Inter-reader agreement is around 50%, while intra-reader agreement is 60-74% (13). The use of AI in radiology and computer-aided diagnosis (CAD) systems is expected to increase inter-reader agreement and improve PCa detection rates in MpMRI.

Radiomics is a library that enables the high-throughput analysis of quantitative radiological features in medical imaging and forms the foundation for AI use in PCa management (14). In MpMRI, ML preprocesses prostate images and performs segmentation. Lesions are detected and classified in the recorded prostate image. The PI-RADS classification generated through ML analysis, predominantly based on T2-weighted and diffusion-weighted imaging (DWI) in MpMRI, is verified by an experienced radiologist. This can reduce the need for experienced radiologists and alleviate their workload. Additionally, AI can improve reproducibility between radiologists and be used as an independent reader. However, experienced radiologists are also needed to input verified data for AI training and to validate the results generated by AI. Another challenge that complicates AI learning is data heterogeneity arising from variations in MpMRI acquisition (15).

Clinical studies and meta-analyses have shown that AI can perform on par with radiologists in detecting PCa in MpMRI, particularly with CAD systems. The benefits of using AI in MpMRI extend beyond lesion detection. AI can provide information about tumor characterization and aggressiveness, significantly reducing the time radiologists spend interpreting images. In studies on prostate segmentation, a similarity coefficient of 0.88-0.93 was achieved between manual segmentation and AI-based segmentations (16,17). In a study on AI-based lesion detection in MpMRI, a sensitivity of 78% was found for index lesions with PI-RADS ≥3. For less experienced radiologists, detection sensitivity for transitional zone lesions was 66.9%, while this rate increased to 83.8% with CAD. Moreover, with CAD assistance, the MRI reading time for experienced radiologists decreased from 3.5 minutes to 2.7 minutes, and for moderately experienced radiologists, it decreased from 6.3 minutes to 4.4 minutes (18). In a study by Song et al. with 195 patients, AI demonstrated an 87% sensitivity in lesion detection (19). In another study comparing histopathological diagnosis, AI detected the index lesion with 3.4% lower sensitivity and clinically significant lesions with 1.5% lower sensitivity than experienced radiologists (20). In a study with 364 patients, Le et al. found that AI showed 100% sensitivity and 76.9% specificity in distinguishing clinically significant and insignificant cancer (21). In a study by Giannini et al., prostate segmentation and lesion detection were performed in MRI images of 131 patients, divided into training and validation groups, using CAD, and verified with pathology. The CAD system did not classify any aggressive tumors as benign, and the area under the curve (AUC) was found to be 0.96 in the training arm and 0.81 in the validation arm (22). On the other hand, Mehralivand et al., in a multicenter study involving nine radiologists with varying levels of experience, found that AI did not significantly improve the performance of less experienced radiologists and had no noticeable effect on inter-reader disagreement. However, a significantly higher sensitivity for transitional zone lesions was detected for AI (23). In a recently conducted large multicenter study, AI demonstrated 94.3% sensitivity in predicting csPCa (24). These studies are promising for personalized disease management in PCa patients using automatic CAD systems.

Prostate Biopsy and Artificial Intelligence

With the incorporation of MpMRI into routine practice for PCa management, fusion MRI-TB is recommended to increase diagnostic accuracy when suspicious lesions are present (25). AI applications used in prostate segmentation and lesion detection in MpMRI can be automatically combined with TRUS images for biopsy, increasing the precision of targeted biopsies and making the process more feasible for radiologists and urologists (26).

For fusion MRI-TB, accurately combining the TRUS image with target lesions and localizing the biopsy needles is of critical importance. In a retrospective study by Mehrtash et al., the needle trajectory was labeled in 71 patients who underwent MRI-TB, and this data was used for AI learning. Validation was conducted on 21 patients who had not been seen by the AI. They achieved accuracy with an acceptable error of 0.98 degree in the needle trajectory (27). Wang et al. in their prospective randomized controlled study compared targeted 6-core biopsy with AI-assisted prostate ultrasound, systematic biopsy under TRUS guidance, and cognitive fusion MRI combined biopsy. In this multicenter study, the detection rate of PCa and csPCA was found to be higher in biopsies performed with AI-assisted prostate ultrasound guidance (28). Anas et al. achieved similar accuracy to offline segmentations by performing real-time prostate segmentation during MRI-TB using AI (29). Real-time prostate segmentation enhances the feasibility of the MRI-TB procedure. AI-assisted biopsy has also been used in nerve-sparing robot-assisted radical prostatectomy for locally advanced PCa. After the prostate is removed, the presence of tumors in the neurovascular bundle is evaluated using a three-dimensional automatic augmented reality system, and selective excisional biopsy is performed. The presence and location of lesions in the neurovascular bundle were correctly identified with 87.5% accuracy. This AI-based application may allow for nerve-sparing surgery in locally advanced disease without compromising oncological outcomes (30).

Histopathological Evaluation and Artificial Intelligence

The gold standard method for diagnosing PCa is histopathological examination, which relies on scoring biopsy material according to the Gleason grading system. This method categorizes tumors into risk groups and provides information about prognosis. However, there is low inter-reader agreement in histopathological scoring systems for PCa diagnosis, similar to what is observed in MpMRI. Studies indicate that the rate of discordance among pathologists ranges from 30% to 53% (31). Instead of microscopic examination, digital histological images offer the possibility of evaluation through CAD tools in various settings, aiming to reduce workforce demands and increase efficiency (32).

The use of AI in digital pathology is primarily focused on the Gleason grading system. Studies involving AI have evaluated the agreement with pathologists and the sensitivity of the system. Arvanti et al. reported a sensitivity of 70% when classifying tissues as benign and Gleason grades 3-5 in the evaluation of tissue microarrays by AI. Moreover, the agreement between the AI model and pathologist interpretations was also found to be high (kappa, 0.71-0.75) (33). In a study where slide images of prostatectomy material were graded for Gleason scores using a developed DL method on 311 slides, a sensitivity of 70% was identified (34). Subsequently, Karimi et al. achieved 92% accuracy in distinguishing benign tissue from malignant tissue and 90% accuracy in differentiating low and high-risk Gleason grades using their designed DL method. In an evaluation using 5,759 biopsy samples from 1,243 patients, the AI model demonstrated superior performance with a kappa score of 0.854, compared to 15 pathologists (35).

Shao et al. evaluated an AI model that analyzes digital pathology images of 502 patients who underwent radical prostatectomy and did not receive additional treatment, all of whom had long follow-up periods. They compared this AI model to risk classification nomograms for predicting biochemical recurrence. The AI model reclassified 3.9% of patients who were classified as low-risk in conventional nomograms as high-risk, while 21.3% of patients classified as high-risk were reclassified as low-risk. The authors noted that having this information post-radical prostatectomy would lead to different treatment approaches and patient counseling (36). In a recent study, 1,279 slides obtained from prostate biopsies were digitized and validated for use in AI learning. The developed AI model was integrated into routine clinical practice for three years, serving as a second-read system for biopsy material in approximately 9,200 patients. The AI model demonstrated 96.7% specificity and 96.6% sensitivity in detecting PCa, while showing 82.1% specificity and 81.1%

sensitivity in distinguishing low-risk PCa from intermediate-high risk PCa (37). AI-based models used in Gleason grading, which is one of the most important prognostic factors in PCa, assist pathologists by improving diagnostic performance.

CONCLUSION

AI, that is increasingly being used and gaining importance in the diagnosis and management of PCa, shows promise in reducing the workload and increasing the efficiency of urologists, pathologists, and radiologists. Studies have shown that AI achieves similar success to radiologists in lesion detection during MpMRI interpretation, enhances the applicability of MRI-TB, and improves concordance among pathologists during histopathological examination. It may also help mitigate potential shortcomings of less experienced clinicians. With large-sample, standardized studies conducted through collaboration between healthcare professionals and technology developers, the effectiveness of AI in improved patient outcomes and personalized patient management in PCa should be clearly demonstrated.

REFERENCES

1. Culp MB, Soerjomataram I, Efstathiou JA, Bray F, Jemal A. Recent Global Patterns in Prostate Cancer Incidence and Mortality Rates. Eur Urol. 2020;77(1):38-52. https://doi.org/10.1016/j.eururo.2019.08.005
2. Schoots IG, Padhani AR, Rouvière O, Barentsz JO, Richenberg J. Analysis of Magnetic Resonance Imaging-directed Biopsy Strategies for Changing the Paradigm of Prostate Cancer Diagnosis. Eur Urol Oncol. 2020;3(1):32-41. https://doi.org/10.1016/j.euo.2019.10.001
3. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA; Grading Committee. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of Grading Patterns and Proposal for a New Grading System. Am J Surg Pathol. 2016;40(2):244-52. https://doi.org/10.1097/PAS.0000000000000530
4. Barbieri CE, Bangma CH, Bjartell A, Catto JW, Culig Z, Grönberg H, Luo J, Visakorpi T, Rubin MA. The mutational landscape of prostate cancer. Eur Urol. 2013;64(4):567-76. https://doi.org/10.1016/j.eururo.2013.05.029
5. Rosenkrantz AB, Ginocchio LA, Cornfeld D, Froemming AT, Gupta RT, Turkbey B, Westphalen AC, Babb JS, Margolis DJ. Interobserver Reproducibility of the PI-RADS Version 2 Lexicon: A Multicenter Study of Six Experienced Prostate Radiologists. Radiology. 2016;280(3):793-804. https://doi.org/10.1148/radiol.2016152542
6. Egevad L, Ahmad AS, Algaba F, Berney DM, Boccon-Gibod L, Compérat E, Evans AJ, Griffiths D, Grobholz R, Kristiansen G, Langner C, Lopez-Beltran A, Montironi R, Moss S, Oliveira P, Vainer B, Varma M, Camparo P. Standardization of Gleason grading among 337 European pathologists. Histopathology. 2013;62(2):247-56. https://doi.org/10.1111/his.12008
7. Goldenberg SL, Nir G, Salcudean SE. A new era: artificial intelligence and machine learning in prostate cancer. Nat Rev Urol. 2019;16(7):391-403. https://doi.org/10.1038/s41585-019-0193-3
8. Sherafatmandjoo H, Safaei AA, Ghaderi F, Allameh F. Prostate cancer diagnosis based on multi-parametric MRI, clinical and pathological factors using deep learning. Sci Rep. 2024 Jun 28;14(1):14951. https://doi.org/10.1038/s41598-024-65354-0
9. Porpiglia F, Manfredi M, Mele F, Cossu M, Bollito E, Veltri A, Cirillo S, Regge D, Faletti R, Passera R, Fiori C, De Luca S. Diagnostic Pathway with Multiparametric Magnetic Resonance Imaging Versus Standard Pathway: Results from a Randomized Prospective Study in Biopsy-naïve Patients with Suspected Prostate Cancer. Eur Urol. 2017;72(2):282-288. https://doi.org/10.1016/j.eururo.2016.08.041
10. Cacciamani GE, Sanford DI, Chu TN, Kaneko M, De Castro Abreu AL, Duddalwar V, Gill IS. Is Artificial Intelligence Replacing Our Radiology Stars? Not Yet! Eur Urol Open Sci. 2022 Dec 19;48:14-16. https://doi.org/10.1016/j.euros.2022.09.024
11. Rosenkrantz AB, Ayoola A, Hoffman D, Khasgiwala A, Prabhu V, Smereka P, Somberg M, Taneja SS. The Learning Curve in Prostate MRI Interpretation: Self-Directed Learning Versus Continual Reader Feedback. AJR Am J Roentgenol. 2017;208(3):W92-W100. https://doi.org/10.2214/AJR.16.16876
12. Richenberg J, Løgager V, Panebianco V, Rouviere O, Villeirs G, Schoots IG. The primacy of multiparametric MRI in men with suspected prostate cancer. Eur Radiol. 2019;29(12):6940-6952. https://doi.org/10.1007/s00330-

019-06166-z

13. Smith CP, Harmon SA, Barrett T, Bittencourt LK, Law YM, Shebel H, An JY, Czarniecki M, Mehralivand S, Coskun M, Wood BJ, Pinto PA, Shih JH, Choyke PL, Turkbey B. Intra- and interreader reproducibility of PI-RADSv2: A multireader study. J Magn Reson Imaging. 2019;49(6):1694-1703. https://doi.org/10.1002/jmri.26555

14. Sugano D, Sanford D, Abreu A, Duddalwar V, Gill I, Cacciamani GE. Impact of radiomics on prostate cancer detection: a systematic review of clinical applications. Curr Opin Urol. 2020;30(6):754-781. https://doi.org/10.1097/MOU.0000000000000822

15. Mata LA, Retamero JA, Gupta RT, García Figueras R, Luna A. Artificial Intelligence-assisted Prostate Cancer Diagnosis: Radiologic-Pathologic Correlation. Radiographics. 2021;41(6):1676-1697. https://doi.org/10.1148/rg.2021210020

16. Wang B, Lei Y, Tian S, Wang T, Liu Y, Patel P, Jani AB, Mao H, Curran WJ, Liu T, Yang X. Deeply supervised 3D fully convolutional networks with group dilated convolution for automatic MRI prostate segmentation. Med Phys. 2019;46(4):1707-1718. https://doi.org/10.1002/mp.13416

17. Sanford TH, Zhang L, Harmon SA, Sackett J, Yang D, Roth H, Xu Z, Kesani D, Mehralivand S, Baroni RH, Barrett T, Girometti R, Oto A, Purysko AS, Xu S, Pinto PA, Xu D, Wood BJ, Choyke PL, Turkbey B. Data Augmentation and Transfer Learning to Improve Generalizability of an Automated Prostate Segmentation Model. AJR Am J Roentgenol. 2020;215(6):1403-1410. https://doi.org/10.2214/AJR.19.22347

18. Gaur S, Lay N, Harmon SA, Doddakashi S, Mehralivand S, Argun B, Barrett T, Bednarova S, Girometti R, Karaarslan E, Kural AR, Oto A, Purysko AS, Antic T, Magi-Galluzzi C, Saglican Y, Sioletic S, Warren AY, Bittencourt L, Fütterer JJ, Gupta RT, Kabakus I, Law YM, Margolis DJ, Shebel H, Westphalen AC, Wood BJ, Pinto PA, Shih JH, Choyke PL, Summers RM, Turkbey B. Can computer-aided diagnosis assist in the identification of prostate cancer on prostate MRI? a multi-center, multi-reader investigation. Oncotarget. 2018 Sep 18;9(73):33804-33817. https://doi.org/10.18632/oncotarget.26100

19. Mehrtash A, Sedghi A, Ghafoorian M, Taghipour M, Tempany CM, Wells WM 3rd, Kapur T, Mousavi P, Abolmaesumi P, Fedorov A. Classification of Clinical Significance of MRI Prostate Findings Using 3D Convolutional Neural Networks. Proc SPIE Int Soc Opt Eng. 2017 Feb 11;10134:101342A. https://doi.org/10.1117/12.2277123

20. Cao R, Mohammadian Bajgiran A, Afshari Mirak S, Shakeri S, Zhong X, Enzmann D, Raman S, Sung K. Joint Prostate Cancer Detection and Gleason Score Prediction in mp-MRI via FocalNet. IEEE Trans Med Imaging. 2019;38(11):2496-2506. https://doi.org/10.1109/TMI.2019.2901928

21. Le MH, Chen J, Wang L, Wang Z, Liu W, Cheng KT, Yang X. Automated diagnosis of prostate cancer in multi-parametric MRI based on multimodal convolutional neural networks. Phys Med Biol. 2017 Jul 24;62(16):6497-6514. https://doi.org/10.1088/1361-6560/aa7731

22. Giannini V, Mazzetti S, Defeudis A, Stranieri G, Calandri M, Bollito E, Bosco M, Porpiglia F, Manfredi M, De Pascale A, Veltri A, Russo F, Regge D. A Fully Automatic Artificial Intelligence System Able to Detect and Characterize Prostate Cancer Using Multiparametric MRI: Multicenter and Multi-Scanner Validation. Front Oncol. 2021 Oct 1;11:718155. https://doi.org/10.3389/fonc.2021.718155

23. Mehralivand S, Harmon SA, Shih JH, Smith CP, Lay N, Argun B, Bednarova S, Baroni RH, Canda AE, Ercan K, Girometti R, Karaarslan E, Kural AR, Purysko AS, Rais-Bahrami S, Tonso VM, Magi-Galluzzi C, Gordetsky JB, Macarenco RSES, Merino MJ, Gumuskaya B, Saglican Y, Sioletic S, Warren AY, Barrett T, Bittencourt L, Coskun M, Knauss C, Law YM, Malayeri AA, Margolis DJ, Marko J, Yakar D, Wood BJ, Pinto PA, Choyke PL, Summers RM, Turkbey B. Multicenter Multireader Evaluation of an Artificial Intelligence-Based Attention Mapping System for the Detection of Prostate Cancer With Multiparametric MRI. AJR Am J Roentgenol. 2020;215(4):903-912. https://doi.org/10.2214/AJR.19.22573

24. Sun Z, Wang K, Wu C, Chen Y, Kong Z, She L, Song B, Luo N, Wu P, Wang X, Zhang X, Wang X. Using an artificial intelligence model to detect and localize visible clinically significant prostate cancer in prostate magnetic resonance imaging: a multicenter external validation study. Quant Imaging Med Surg. 2024 Jan 3;14(1):43-60. https://doi.org/10.21037/qims-23-791

25. Mottet N, van den Bergh RCN, Briers E, Van den Broeck

T, Cumberbatch MG, De Santis M, Fanti S, Fossati N, Gandaglia G, Gillessen S, Grivas N, Grummet J, Henry AM, van der Kwast TH, Lam TB, Lardas M, Liew M, Mason MD, Moris L, Oprea-Lager DE, van der Poel HG, Rouvière O, Schoots IG, Tilki D, Wiegel T, Willemse PM, Cornford P. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol. 2021;79(2):243-262. https://doi.org/10.1016/j.eururo.2020.09.042

26. van Sloun RJG, Wildeboer RR, Mannaerts CK, Postema AW, Gayet M, Beerlage HP, Salomon G, Wijkstra H, Mischi M. Deep Learning for Real-time, Automatic, and Scanner-adapted Prostate (Zone) Segmentation of Transrectal Ultrasound, for Example, Magnetic Resonance Imaging-transrectal Ultrasound Fusion Prostate Biopsy. Eur Urol Focus. 2021;7(1):78-85. https://doi.org/10.1016/j.euf.2019.04.009

27. Mehrtash A, Ghafoorian M, Pernelle G, Ziaei A, Heslinga FG, Tuncali K, Fedorov A, Kikinis R, Tempany CM, Wells WM, Abolmaesumi P, Kapur T. Automatic Needle Segmentation and Localization in MRI With 3-D Convolutional Neural Networks: Application to MRI-Targeted Prostate Biopsy. IEEE Trans Med Imaging. 2019;38(4):1026-1036. https://doi.org/10.1109/TMI.2018.2876796

28. Wang X, Xie Y, Zheng X, Liu B, Chen H, Li J, Ma X, Xiang J, Weng G, Zhu W, Wang G, Fang Y, Cheng H, Xie L. A prospective multi-center randomized comparative trial evaluating outcomes of transrectal ultrasound (TRUS)-guided 12-core systematic biopsy, mpMRI-targeted 12-core biopsy, and artificial intelligence ultrasound of prostate (AIUSP) 6-core targeted biopsy for prostate cancer diagnosis. World J Urol. 2023;41(3):653-662. https://doi.org/10.1007/s00345-022-04086-0

29. Ling JQ, Mao J. [State of the art and perspective of pulp regeneration]. Zhonghua Kou Qiang Yi Xue Za Zhi. 2018 Jun 9;53(6):361-366. Chinese. https://doi.org/10.3760/cma.j.issn.1002-0098.2018.06.001

30. Checcucci E, Piana A, Volpi G, Piazzolla P, Amparore D, De Cillis S, Piramide F, Gatti C, Stura I, Bollito E, Massa F, Di Dio M, Fiori C, Porpiglia F. Three-dimensional automatic artificial intelligence driven augmented-reality selective biopsy during nerve-sparing robot-assisted radical prostatectomy: A feasibility and accuracy study. Asian J Urol. 2023;10(4):407-415. https://doi.org/10.1016/j.ajur.2023.08.001

31. Allsbrook WC Jr, Mangold KA, Johnson MH, Lane RB, Lane CG, Epstein JI. Interobserver reproducibility of Gleason grading of prostatic carcinoma: general pathologist. Hum Pathol. 2001;32(1):81-8. https://doi.org/10.1053/hupa.2001.21135

32. Retamero JA, Aneiros-Fernandez J, Del Moral RG. Complete Digital Pathology for Routine Histopathology Diagnosis in a Multicenter Hospital Network. Arch Pathol Lab Med. 2020;144(2):221-228. https://doi.org/10.5858/arpa.2018-0541-OA

33. Arvaniti E, Fricker KS, Moret M, Rupp N, Hermanns T, Fankhauser C, Wey N, Wild PJ, Rüschoff JH, Claassen M. Automated Gleason grading of prostate cancer tissue microarrays via deep learning. Sci Rep. 2018 Aug 13;8(1):12054. https://doi.org/10.1038/s41598-018-30535-1

34. Nagpal K, Foote D, Liu Y, Chen PC, Wulczyn E, Tan F, Olson N, Smith JL, Mohtashamian A, Wren JH, Corrado GS, MacDonald R, Peng LH, Amin MB, Evans AJ, Sangoi AR, Mermel CH, Hipp JD, Stumpe MC. Development and validation of a deep learning algorithm for improving Gleason scoring of prostate cancer. NPJ Digit Med. 2019 Jun 7;2:48. https://doi.org/10.1038/s41746-019-0112-2

35. Bulten W, Pinckaers H, van Boven H, Vink R, de Bel T, van Ginneken B, van der Laak J, Hulsbergen-van de Kaa C, Litjens G. Automated deep-learning system for Gleason grading of prostate cancer using biopsies: a diagnostic study. Lancet Oncol. 2020;21(2):233-241. https://doi.org/10.1016/S1470-2045(19)30739-9

36. Shao Y, Bazargani R, Karimi D, Wang J, Fazli L, Goldenberg SL, Gleave ME, Black PC, Bashashati A, Salcudean S. Prostate Cancer Risk Stratification by Digital Histopathology and Deep Learning. JCO Clin Cancer Inform. 2024;8:e2300184. https://doi.org/10.1200/CCI.23.00184

37. Santa-Rosario JC, Gustafson EA, Sanabria Bellassai DE, Gustafson PE, de Socarraz M. Validation and three years of clinical experience in using an artificial intelligence algorithm as a second read system for prostate cancer diagnosis-real-world experience. J Pathol Inform. 2024 Apr 30;15:100378. https://doi.org/10.1016/j.jpi.2024.100378