*Asian Journal of Biology*

***Volume 20, Issue 10, Page 49-64, 2024; Article no.AJOB.123994***
***ISSN: 2456-7124***

# Advancing Prostate Cancer Diagnosis and Treatment Through AI-Driven Decision-making: A Comprehensive PRISMA-Based Systematic Review

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

***Article Information***

DOI: https://doi.org/10.9734/ajob/2024/v20i10443

**Open Peer Review History:**
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/123994

***Systematic Review Article***

***Received: 21/07/2024***
***Accepted: 24/09/2024***
***Published: 02/10/2024***

## ABSTRACT

Decision-making during the diagnosis and treatment of prostate cancer often requires the evaluation of data from several sources. The purpose of this systematic was to evaluate how AI can enhance prostate cancer diagnosis and treatment. We search five different databases for available

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***Cite as:*** *Choudhary, Rohit, Santi Swarup Swain, Anshul Khairari, Priyabrata Thatoi, and Hrudayanath Thatoi. 2024. "Advancing Prostate Cancer Diagnosis and Treatment Through AI-Driven Decision-Making: A Comprehensive PRISMA-Based Systematic Review". Asian Journal of Biology 20 (10):49-64. https://doi.org/10.9734/ajob/2024/v20i10443.*

studies using a pre-specified search strategy. The study was conducted using PRISMA guidelines. A total of 1058 studies were found on five different databases (Scopus N=287, Web of Science N=204, PubMed/EMBASE N=306, Cochrane Library N=94, Google Scholar N=167). The articles were stored in the ENDNOTE library and all the duplicates were removed. We found 19 relevant studies that were included after a stringent assessment criterion based on the inclusion and exclusion criteria. Included studies were assessed for risk bias assessment using the Newcastle Ottawa Scale (NOS) in which one study was found to have high-risk bias assessment, seven were identified to have low-risk bias assessment while the rest of the studies were moderate. Clinicians can recognize complex correlations and handle massive data sets with the help of artificial intelligence. These tasks are extremely laborious and challenging for humans to complete. It is feasible to employ fewer resources while increasing overall effectiveness and precision in prostate cancer detection and treatment by utilizing AI algorithms and lowering the degree of subjectivity. This review provides a comprehensive comparison of AI algorithms in detection of prostate cancer.

*Keywords: Artificial intelligence; prostate cancer; artificial neural network; machine learning.*

## 1. INTRODUCTION

With an expected of 1.4 million cases expected in 2024, prostate carcinoma is the 2nd most common malignancy among men worldwide [1]. Prostate cancer is predicted to cause 299,010 incident cases and 35,250 deaths by the year 2024 [2]. Prostate cancer mortality makes up only 10% of all cancer fatalities, despite the disease's high incidence. The five-year rate of survival for all stages of prostate cancer combined is more than 98% [3]. Prostate cancer often presents without noticeable symptoms in its early stages, which is why regular screening is crucial. However, as the disease progresses, men may experience symptoms such as difficulty urinating, a weak or interrupted urine flow, the need to urinate frequently (especially at night), blood in urine or semen, erectile dysfunction, or discomfort in the pelvic area. In more advanced cases, bone pain or swelling in the legs can indicate that the cancer has spread. It's important to consult a healthcare provider for regular screenings, particularly if any of these symptoms occur. With the high incidence of prostate cancer and low death rate, it is critical to accurately distinguish between aggressive and non-aggressive forms of the disease to reduce overdiagnosis and excessive treatment. The application of artificial intelligence approaches has the potential to significantly improve the management of prostate cancer by highlighting key traits that are diagnostic of the disease [4].

Various large prospective studies conducted in the years 2018 and 2019 found that, when compared with a transrectal ultrasound-assisted biopsy, the application of Magnetic Resonance Imaging (MRI) before a biopsy improves the detection of (aggressive) clinically important prostate cancer while reducing the detection of (mild) minor prostate cancer [5]. Because of this, the European Association of Urology has included multiparametric MRI in its list of recommended tests, which must be completed before a biopsy. Reporting prostate MRIs should be done using the Prostate Imaging and Reporting and Monitoring System. A Likert scale with five points is used to rank suspicious growths for prostate cancer, ranging from extremely unlikely to highly probable [6].

The AI paradigm has changed significantly as a result of increased access to vast volumes of healthcare data, enhanced computation and infrastructure capabilities, advancements in machine vision models, and the introduction of large language models (LLMs) [7]. LLMs can significantly reduce operational and documentation costs, speed up drug discovery, and change precision oncology and clinical trials due to their generative and reasoning abilities [2]. Prostate cancer is a cancer with diverse presentation, clinical results, and therapeutic options, making it especially pertinent to customize therapies based on individual patient profiles [8].

In order to evaluate the distinction and severity of prostate cancer, image-based procedures including histopathological techniques, magnetic resonance imaging (MRI), and biomarkers diagnostics can be automated with the help of artificial intelligence [9]. Additionally, patients who are diagnosed with prostate cancer may continue to receive repeated monitoring tests, such as prostate-specific antigens, MRIs, and rectal exams, as long as they are not experiencing any physiological complications. Artificial Intelligence has the potential to enhance

these surveillance methods and become an important tool for urology pathologists and the urology community as technology advances and enhances patient outcomes over time. In this systematic review, we review the available literature on how AI can enhance prostate cancer diagnosis and treatment.

## 2. METHODOLOGY

This systematic review of available studies on our topic was conducted according to the PRISMA guidelines ("Preferred Reporting Items for Systematic Reviews and Meta-Analyses") [10].

### 2.1 Search Strategy

We use five different databases for searching published studies in English without the publishing timeframe restriction. The following search strategy were used for each database: **Scopus:** "("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural networks" OR "AI" OR "ML") AND ("prostate cancer" OR "prostatic neoplasms" OR "prostate tumor" OR "prostate carcinoma" OR "prostate adenocarcinoma"), **Web of Science:** TS=("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural networks" OR "AI" OR "ML") AND TS=("prostate cancer" OR "prostatic neoplasms" OR "prostate tumor" OR "prostate carcinoma" OR "prostate adenocarcinoma"), **PubMed/EMBASE:** ("artificial intelligence"[MeSH Terms] OR "machine learning"[MeSH Terms] OR "deep learning"[MeSH Terms] OR "neural networks"[MeSH Terms] OR "AI" OR "ML") AND ("prostate cancer"[MeSH Terms] OR "prostatic neoplasms"[MeSH Terms] OR "prostate tumor" OR "prostate carcinoma" OR "prostate adenocarcinoma"), **Google Scholar:** "artificial intelligence" OR "machine learning" OR "deep learning" OR "neural networks" OR "AI" OR "ML" AND "prostate cancer" OR "prostatic neoplasms" OR "prostate tumor" OR "prostate carcinoma" OR "prostate adenocarcinoma", and **Cochrane Library:** ("artificial intelligence" OR "machine learning" OR "deep learning" OR "neural networks" OR "AI" OR "ML") AND ("prostate cancer" OR "prostatic neoplasms" OR "prostate tumor" OR "prostate carcinoma" OR "prostate adenocarcinoma")". We also checked these databases for the presence of previous or ongoing systematic reviews on the subject. We combined results from different databases and discarded repeated results using Endnote software.

### 2.2 Studies Selection

All articles were extracted and stored in a separate Endnote Library (ENDNOTE, 2015) and duplicates were removed. Studies were selected for inclusion by two different reviewers. Reviewer 1 assessed abstracts and titles in duplicate, separately, while reviewer 2 approved studies based on the data and solved any disagreements on any included study. After the papers were thoroughly reviewed by reviewers, they were selected for inclusion based on the subsequent inclusion and exclusion criteria, which helped establish if the publications contained the necessary data for the systematic review:

**Inclusion Criteria:**

- Randomized control trials, Cohort studies, prospective studies were included in this review.
- Studies that were focused on AI in prostate cancer.
- Studies that report outcomes related to the effectiveness, accuracy, sensitivity, specificity, or clinical utility of AI in prostate cancer.
- Studies that were published in the English language

**Exclusion criteria:**

- Studies that were case reports, systematic reviews, editorial letters, non-comparative studies, and case series were excluded
- Studies without a focus on AI in prostate cancer.
- Studies that do not report relevant outcomes, or where the outcomes are not clearly defined or measurable.
- Studies published in languages other than English

To collect and preserve data and records, a Microsoft® Excel Spreadsheet was utilized (Microsoft, Inc., Redmond, Wash., USA).

### 2.3 Risk Bias Assessment

The Newcastle Ottawa Scale was used to evaluate the included studies. Studies were scored low, medium, and high based on bias in the selection, bias in interventions, bias in deviations interventions, bias because of data missing, bias in outcomes, and bias in results.

Inclusion and exclusion criteria were used for scoring of preference for selection. Performance bias was assessed by accounting for allocation concealment and describing a control arm. Various rankings were given to incomplete industry sponsorship, data management, biased reporting, and selective reporting. Reporting uniformity and eligibility limitations were discussed over several meetings with reviewers. Before choosing a study, a second reviewer took into account any gaps in the reviewers' scoring.

The evidence's quality and certainty were evaluated using GRADE (Grading of Recommendations Assessment, Development, and Evaluation). Regarding quality and certainty, the evidence is categorized as high, moderate, or low. The uncertainty of the evidence (the outcome measure's lack of direct relevance to the purpose of the study), imprecision of the results, the seriousness of inconsistent results, the designs of the included studies, the seriousness of the risk of bias, and other factors like publication bias are all taken into consideration by the GRADE system when evaluating the quality and certainty of included studies.

## 3. RESULTS AND DISCUSSION

### 3.1 Search Results

A total of 1058 studies were found on five different databases. When the studies were sorted on Endnote, 579 studies were excluded as duplicates. 479 studies were screened based on titles and accessibility. Among them, 398 studies were excluded as only the abstract was accessible. 81 full article texts were retrieved and assessed for eligibility in which only 31 studies were found to be eligible for our studies. When these articles were carefully studied, 12 articles were found in which the study was focused only on prostate cancer and not on the application of AI, which was irrelevant and was excluded from the study. The studies were shortened to just 19 original research publications, which were assessed in this systematic review (Fig. 1).

### 3.2 Risk Bias Assessment

Newcastle-Ottawa Scale was utilized to evaluate the risk of bias. 7 studies among the 19 were determined to have low-risk bias, 11 to possess moderate risk bias, and one to exhibit high-risk bias. Some studies have methodological flaws related to the selection of the controls. Moreover, no study revealed how controls and patients were blinded to exposure, which could have caused bias in the measurements (Table 1).

The studies included in the present systematic review exhibited low quality of evidence, according to GRADEpro GDT. The primary reasons for the poor quality of evidence were the presence of a cohort study, which raises the possibility of bias as it cannot randomize the amount of exposure, and the uneven character of the study.

### 3.3 Artificial Neural Network (ANN) and Prostate-Specific Antigens (PSA)

Measuring an increased PSA level is thought to be one of the most popular clinical methods for prostate cancer diagnosis [30]. Nevertheless, several other benign prostatic diseases also have increased PSA levels, which may result in needless predictive treatments [31]. While a prostate-specific antigen level of more than 4 ng/mL is typically taken into consideration for early prostate cancer screening, approximately 20% of men with the disease never reach that cutoff. Using innovative non-invasive techniques, there has been a tremendous demand for diagnosing prostate carcinoma in male with indeterminate prostate specific antigen level to better their health.

Numerous research have evaluated the utility of prostate-specific antigen in conjunction with other clinical parameters inside an ANN for the identification of prostate carcinoma and its growth. For example, Djavan et al. developed an ANN to increase the specificity and accuracy of prostate cancer detection [15]. The primary goal of the 1246-person trial was to ascertain whether males with plasma total Prostate-specific antigen levels within 2.5-4 ng per milliliter and between 4-10 ng per milliliter have benign prostate tissue or prostate cancer in comparison to normal procedures. For people with total prostate specific levels between 4 and 10 ng/mL, the ANN model performed better than all other comparative variables in terms of precision, positive value for prediction, negative prognosis value, and the ROC values at 95% sensitive.

In another investigation, Stojadinovic et al. [26] examined a number of variables and found that PSA concentration was the most important one. They also demonstrated that a decision tree outperformed the logistic regression model in terms of net benefit. The framework used in this

retrospective analysis could lower the number of pointless biopsies without sacrificing important diagnoses. In order to eliminate needless prognostic testing in cases where prostate specific antigen results were mistakenly positive, Finne et al. developed an ANN with free prostate specific antigen [17]. The model was constructed using data from 656 individuals in Finland whose total serum prostate specific antigen levels ranged from 4 to 10 ng/mL. Prostate size, digital examination of rectum, percentage of free prostate specific antigen, and average PSA were among the data. 19% of false-positive PSA results were found to be eliminated by the proportion of free PSA at a 95% sensitivity level, as opposed to 24% by the logistic regression technique and 33% by the ANN. These findings suggest that it is advantageous to use an ANN technique to lower the number of false positives results in the detection of prostate cancer.

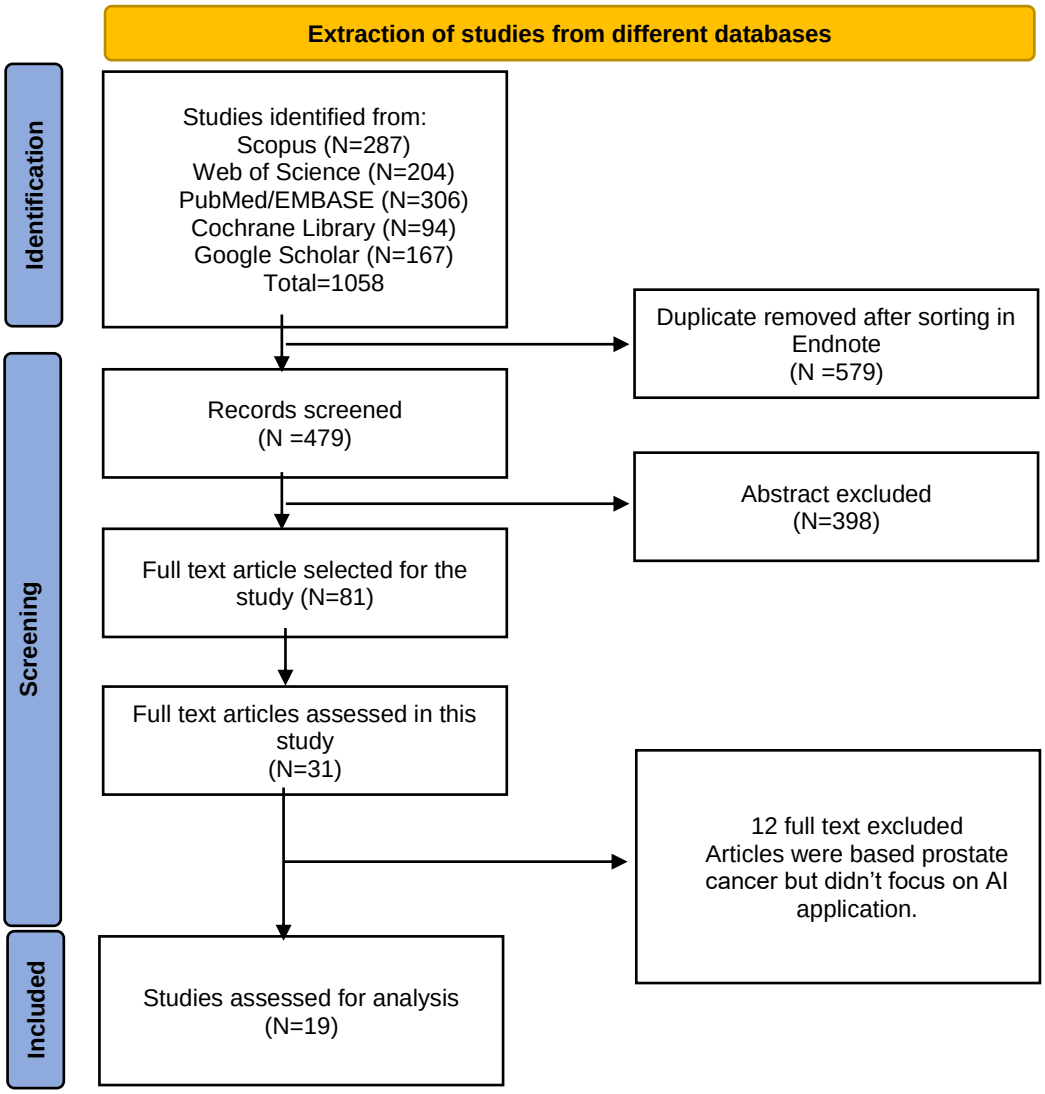


**Fig. 1. PRISMA flow chart for studies selection**

**Table 1. Risk bias assessment of all the studies included in the systematic review on AI in prostate cancer using the Newcastle - Ottawa Scale**

| Study | Selection | | | | Comparability | Exposure | | |
|---|---|---|---|---|---|---|---|---|
| | 1. | 2. | 3. | 4. | 1. | 1. | 2. | 3. |
| (Alitto et al., 2017) [11] | ★ | ★ | | | ★★ | ★ | | ★ |
| (Antonelli et al., 2019) [12] | ★ | ★ | | | ★ | ★ | ★ | |

| Study | Selection | | | | Comparability | Exposure | | |
|---|---|---|---|---|---|---|---|---|
| | 1. | 2. | 3. | 4. | 1. | 1. | 2. | 3. |
| (Auffenberg et al., 2019) [13] | ★ | ★ | | | | ★ | ★ | ★ |
| (Bhele et al., 2014) [14] | ★ | ★ | ★ | | ★★ | ★ | ★ | ★ |
| (Djavan et al., 2002) [15] | ★ | ★ | | | ★★ | ★ | ★ | ★ |
| (Fehr et al., 2015) [16] | ★ | ★ | | | ★ | ★ | ★ | ★ |
| (Finne et al., 2000) [17] | ★ | ★ | | | ★★ | | ★ | ★ |
| (Ge et al., 2015) [18] | ★ | ★ | | ★ | ★★ | ★ | ★ | ★ |
| (Green et al., 2016) [19] | ★ | ★ | ★ | | ★ | | ★ | ★ |
| (Kim et al., 2016) [20] | ★ | ★ | | | ★★ | ★ | ★ | ★ |
| (Kumar et al., 2017) [21] | ★ | ★ | | | | | ★ | |
| (Lawrentschuk et al., 2011) [22] | ★ | ★ | | | | ★ | ★ | ★ |
| (Naguib et al., 1998) [23] | ★ | ★ | ★ | | ★★ | ★ | ★ | ★ |
| (Remzi et al., 2003) [24] | ★ | ★ | ★ | | ★ | ★ | ★ | |
| (Stephan et al., 2002) [25] | ★ | ★ | | | | ★ | ★ | |
| (Stojadinovic et al., 2019) [26] | ★ | ★ | | | ★★ | ★ | ★ | ★ |
| (Strom et al., 2020) [27] | ★ | ★ | | | ★ | ★ | ★ | ★ |
| (Toivonen et al., 2019) [28] | ★ | ★ | | ★ | | ★ | ★ | ★ |
| (Waliszewski et al., 2015) [29] | ★ | ★ | ★ | | ★★ | ★ | ★ | ★ |

*Rating scale: 0 to 3 stars = high risk of bia,; 4 to 6 stars = moderate risk of bias; 7 to 9 stars = low risk of bias*

Ge et al. created an ANN and logistical regression model to help with prostate cancer detection [18]. They trained their algorithms using predictors from 586 individuals whose prostate cancer was confirmed by biopsy, including age, prostate volume, prostate specific antigen density, and percentage free prostate specific antigen. Despite not finding any discernible differences between both models, they came to the conclusion that both had a high degree of diagnostic validity and might be used in clinical settings to reduce the number of needless biopsies.

To identify males at elevated risk of having a positive prostate examination result for cancer, Stephan et al. built an ANN using the percentage of free PSA (%fPSA) [25]. With input data including patient age, volume of prostate, digital rectal exam (DRE) status, total PSA, and percentage, the study included 1188 males with healthy prostates gland or prostate carcinoma. The sensitivity of %fPSA was increased by 20–22% in male with 2 to 10 µg/L overall PSA after using the ANN. Therefore, using an ANN based on %fPSA can reduce the need for needless biopsies and improve detection accuracy compared to using %fPSA alone. The value of utilizing AI-based ANN techniques, which might be successfully combined with some of the essential instruments frequently employed in prostate cancer detection, is demonstrated by several research taken together [32].

### 3.4 ANN and Histopathologic Detection of Prostate Cancer

A prostate tumor diagnosis is frequently dependent on the histological detection of prostatic adenocarcinoma. On the other hand, inter- and intra-observer variation might occasionally lead to histopathologic variability. The introduction of an AI interface to precisely identify, locate, and grade histopathologic slides has been one way to address the issue. The goal of early research, including Bhele et al. [14], was to identify the variations in histology slides between Gleason scores. Prostate cancer aggressiveness can be categorized using the Gleason grading system into low-risk (grade group 1), intermediate-risk (grade groups 2 and 3), and high-risk (grade groups 4 and 5). In this study, a model was trained using 38 samples of radical prostatectomy, producing 105 pictures. The technique achieved 67–81% agreement on G3, G4, and normal epithelium outlines. As a result, the AI model shows a strong potential for differentiating between 3+4 and 4+3 individuals.

In order to train ANNs to evaluate prostate biopsy specimens, Ström et al. used digital slides from 1247 male [27]. Predicting the existence, degree, and Gleason grading of malignant tissue allowed for the evaluation of the networks. In both the independent evaluation data and the validated external the data set, the artificial intelligence tool's area under the receiver

**Table 2. Summarizes the key characteristics of studies included in this systematic review**

| Reference | Publishing Year | Key Objectives | AI Type | Study Summary |
|---|---|---|---|---|
| (Naguib et al., 1998) [23] | 1998 | to evaluate the usefulness of ANNs in prostate cancer outcome prediction as compared to statistical techniques, utilizing a mix of traditional and novel biological markers. | ANN + biomarker dx | Comparing ANN with statistical techniques with both experimental and traditional biomarkers. |
| (Finne et al., 2000) [17] | 2000 | to determine whether the percentage of free Prostate specific antigen in a prostate cancer screening may be used to weed out more false-positive PSA findings using ANN network and logistic regression. | ANN + PSA dx | More so than a free PSA by itself, multivariate algorithms based on clinical features may lower the prostate screening rate of false-positive results. In comparison to a free PSA, the logistic regression model demonstrated greater accuracy and sensitivity, indicating potential to lower the incidence of needless prostate biopsies. |
| (Djavan et al., 2002) [15] | 2002 | The ANN's predicted accuracy was contrasted with the results of traditional statistical analysis using the standard PSA parameters. | ANN + PSA dx | By using PSA values, early prostate cancer can be statistically predicted. Compared to multivariate analysis and traditional PSA parameters, the ANN accuracy level was greater. |
| (Stephan et al., 2002) [25] | 2002 | To assess the diagnostic utility of an ANN based on % free PSA in males whose t-prostate specific antigen concentrations are between 2-20 µg/L in order to identify individuals who are at a higher risk of having a prostate biopsy that confirms cancer. | ANN + PSA dx | Neural networks with artificial intelligence were used to evaluate the diagnostic usefulness of percentage of free PSA in males whose total plasma PSA levels ranged from 2-20 µg/L. When combined with measurements of prostate volume and digital rectal examination, the ANN showed better accuracy than % free prostate screening alone. |
| (Remzi et al., 2003) [24] | 2003 | to create an ANNs to forecast the existence of prostate carcinoma and the results of additional biopsies of prostate. | ANN + PSA dx | Utilizing ANN to forecast recurrence using clinical features, PSA density, and free/total PSA. The ANN decreased needless repeat biopsies by identifying a pattern of prostate carcinoma in males who had a negative prostate initial biopsy. |
| (Lawrentschuk et al., 2011) [22] | 2011 | To develops ANNs and polychotomous logistic regression models to forecast biopsy findings, especially for clinically important prostate cancer. | ANN + histopathologic dx | ANN and the polychotomous logistic regression equation are used to forecast the results of the biopsy. |

| Reference | Publishing Year | Key Objectives | AI Type | Study Summary |
|---|---|---|---|---|
| (Bhele et al., 2014) [14] | 2014 | The study supplemented the Gleason Grading of Prostate Carcinoma with a machine learning method. | ANN + histopathologic dx | Automated picture analysis that captures the architectural variations between different Gleason grades and benign epithelium utilizing methods like to facial recognition. This automated approach demonstrated potential in distinguishing between G3+4 and G4+3 grades and demonstrated concordance with pathologists with training. |
| (Fehr et al., 2015) [16] | 2015 | The paper presents an autonomous ML-based categorization system for prostate cancer aggressiveness, which combines textural data derived from T2-w (T2-weighted) MRI with apparent diffusion coefficient (ADC). | ANN + MRI dx | T2-weighted texture data and the apparent diffusion coefficient are combined in multiparametric MRI image processing. The findings imply that textural features combined with basic data augmentation provide a categorization of Gleason patterns that is reasonably reliable. |
| (Ge et al., 2015) [18] | 2015 | to create two prostate cancer prediction models and evaluate the diagnostic efficacy of each using LR and ANN. | ANN + PSA dx | A comparison of the diagnostic performance of ANNs versus logistic regression. Both algorithms' alignment revealed no discernible difference between the two outcomes. |
| (Waliszewski et al., 2015) [29] | 2015 | to investigate the connection between the intricacy of the prostate cancer cell nuclei's spatial distribution and the tumor's structure. | ANN + histopathologic dx | Adenocarcinoma stratification according on histological analysis of tumor architecture. After complex patterns were categorized and stratified, there was a decrease in intraobserver variability, which made it more appropriate to advise patients to undergo active surveillance. |
| (Green et al., 2016) [19] | 2016 | to identify male who are most at risk of death young from prostate carcinoma and to verify biomarkers for prognosticating the disease's outcomes using reliable and commonly used pathology procedures. | ANN + biomarker dx | predictive biomarkers for KI67 and DLX2 outcomes. Both demonstrated usefulness in supporting clinical judgments made on patients undergoing active surveillance. |
| (Kim et al., 2016) [20] | 2016 | To use machine learning and tailored proteomics to find accurate proteome indicators for prostate cancer. | ANN + biomarker dx | Prostate cancer strong proteomic markers can be found by targeted proteomics. Using computationally guided the field of proteomics highly precise non-invasive biomarkers can be found. |

| Reference | Publishing Year | Key Objectives | AI Type | Study Summary |
|---|---|---|---|---|
| (Alitto et al., 2017) [11] | 2017 | The study proposes an umbrella protocol, with an emphasis on prostate cancer, to facilitate the development of multifactorial DSSs (Decision Support Systems). | ANN + risk classification | Suggested umbrella protocol that harmonizes processes and data to produce a standardized dataset that may be utilized to develop sophisticated decision support systems. This application thus facilitates the use of multivariate data sources for individualized decision making. |
| (Kumar et al., 2017) [21] | 2017 | The study presents a method for using tissue pictures to predict the return of prostate carcinoma following a radical prostatectomy. | ANN + risk stratification | Processing of images used for being able to detect recurrence using H&E slides. When applied to 30 cases that recur and 30 non-recurrent cases, two level CNN exhibits good accuracy. This might be used to select treatment alternatives according to slides. |
| (Antonelli et al., 2019) [12] | 2019 | The goal of the study was to ascertain if prostate cancers with or without a Gleason 4 component could be reliably classified using ML classifiers for the area of transition and periphery zone. Furthermore, the performance of the top-performing classifiers was contrasted with the assessments of three board-certified radiologists. | ANN + MRI dx | In order to categorize prostate cancers with or without a Gleason 4 element, ML classifiers for the transition zone and outer zone in MRI images were tested. Classifiers that were trained inside each zone performed better than the pathologists' option. |
| (Auffenberg et al., 2019) [13] | 2019 | To use a prostate cancers registry to build a platform on the internet that lets men who have just received a diagnosis see treatment suggestions according to patients who have similar characteristics. | ANN + patient interaction | Clinical registry to facilitate patient interaction with similarity-based therapy decisions. Patients who have just received a diagnosis can research their alternatives and contrast their suggested course of care with those of other patients receiving comparable care. |
| (Stojadinovic et al., 2019) [26] | 2019 | To create a model known as the CART (classification and regression tree) that would be used to determine whether patients had advanced prostate carcinoma. | ANN + PSA dx | Create a regression tree and classification system that can be used to determine which people have prostate cancer that is significant based on the results of a digital examination of the rectum, an aberrant PSA, or both. When contrasted with a logistic regression model, prostate-specific antigen density, and biopsying every patient, the analysis revealed a net advantage. |

| Reference | Publishing Year | Key Objectives | AI Type | Study Summary |
|---|---|---|---|---|
| (Toivonen et al., 2019) [28] | 2019 | The objective was to develop and validate a classifier system that predicts the Gleason score for cancer of the prostate using radiomic and texture data from T2-W images, diffuse weighted imaging with high b values, and T2-mapping. | ANN + MRI dx | This is a classifier system that utilizes texture information from T2-weighted imaging in MRI scans to guess/predict the Gleason score for prostate cancer. The examination of texture features demonstrated strong GS classification performance in prostate cancer cases. |
| (Strom et al., 2020) [27] | 2020 | to create an artificial intelligence system that can identify, locate, and grade prostate cancer with a level of accuracy that is clinically acceptable. | ANN + histopathologic dx | In comparison to skilled urological pathologists, the study assessed ANNs' ability to analyze prostate samples based on the presence and Gleason grade of the cancerous tissue. Based on the findings, urological pathologists and artificial neural networks (ANNs) can be trained to recognize and evaluate prostate biopsies with comparable accuracy. |

operator curve (ROC curve) for differentiating between malignant and benign biopsy cores was 0.997 and 0.986, respectively. These findings were on par with the precision of a global prostate pathology specialist. Such an AI system can offer pathology expertise and a consistent grading scheme to underprivileged areas.

Lawrentschuk et al. [22] conducted a study wherein they constructed a polychotomous logistical regression model and ANN to forecast the biopsy outcomes of 3025 men who had PSA levels less than 10ng/dL. During the developing process, clinical predictors of prostate volume, age, prostate specific antigen, abnormal digital examination of rectum, and positive TRUS (transrectal ultrasonography) were also taken into account. The models' performance was said to be enhanced with the addition of more variables, however the artificial neural network was unable to discern among the 4 biopsy outcomes used in the models' validation. The authors advise using ANN with a more restrained excitement and emphasize the importance of properly training them for efficient use [33].

ANN was created in a different investigation by Remzi et al. to forecast the outcome of repeat biopsies and the existence of prostate cancer [24]. Data from 820 males with readings between 4 and 10 ng/mL were used to build this model. The data included age, f/t PSA ratio, findings from the digital examination of rectum, prostate specific antigen movement, and transrectal ultrasound-guided parameters such as prostate volume, the zone of transformation volume, PSA-TZ, and PSAD. In patients whose initial biopsy resulted in a negative result, a neural network model demonstrated a robust predictive pattern for prostate carcinoma. The ANN's overall performance was 95% sensitivity and 68% specificity [24]. Numerous studies taken together demonstrate the potential for artificial intelligence ANNs to enable more precise patient counseling and the resolution of histopathologic variability.

### 3.5 ANN and MRI Diagnosis for Prostate Cancer

The use of MRI to detect and assess the severity of prostate cancer has been studied. Though their application is still debatable, MR spectroscopy T2-W MRI and ADC (apparent diffusion coefficients) have proven to be useful methods for evaluating prostate cancer [34,35]. Expert users can quickly identify malignant tumors with these methods; nevertheless, it is more challenging to reliably use MRI to determine the tumors' aggressiveness. Consequently, the use of machine learning for automatic classification has been suggested as a way to deliver more reliable and precise results to support doctors in their care. Similar to this, Fehr et al. suggested a method of combining textural data derived from T2-weighted MRI and apparent diffusion coefficients (ADC) for a machine learning-based automated detection of prostate cancer severity [16]. This method was able to distinguish between 3+4 and 4+3 tumors, as well as between low GS6 and high GS (>7) malignancies. Additionally, for tumors that occurred in both the peripheral and transition zones, this model was able to differentiate between high and low Gleason grades with 93% accuracy, and for cancers that only occurred in the PZ, it could do so with 92% accuracy. These outcomes were noticeably better than those obtained with ADC alone, indicating that this approach may be able to classify Gleason patterns with some degree of accuracy.

Furthermore, the authors of a different study by Antonelli et al. built machine learning classifiers using 164 men's clinical characteristics and quantitative MRI data [12]. After the model was validated, these classifiers outperformed the three certified by the board radiologists who took part in the study in terms of accuracy when predicting Gleason four in prostate cancers. It was proposed that these AI classifier tools would be helpful in making decisions about active surveillance programs and in non-invasively monitoring the growth of malignancies [12].

In another investigation, Toivonen et al. designed an ML methods for detecting prostate carcinoma aggressive nature using high-quality, optimized imaging data sets [28]. A classifier system was created employing multi-texture features from diffusion-weighted MRI, high-quality T2-W images, and T2-W relaxation mappings from 100 participants in order to predict prostate cancer. There were two categories for the Gleason score: 3+3 (with a low risk) and greater than3+3 (a high risk). The results showed that textural feature analysis of the DWI, followed by processing utilizing mono-exponential plus kurtosis models, and T2w, successfully categorized the Gleason score of

cancer of the prostate. When taken as a whole, this numerous research demonstrates how AI ANNs may be able to integrate more successfully with contemporary surveillance instruments like MRI to support prostate cancer surveillance.

### 3.6 ANN in Diagnosis of Biomarkers

Prostate-specific antigen testing has influenced prostate cancer detection and prognosis. On the other hand, patients may be offered intrusive treatment alternatives when continuous monitoring could yield superior results for these men due to worries about absolute accuracy [36]. A plethora of biomarkers have been discovered and included in clinical assays throughout the last ten years [37,38,39]. Because of the unique functions of each test, there is no universal set of biomarkers to consider when making a diagnosis or prognosis, even though many of these indicators have been researched and documented. Therefore, it is critical to be able to accurately and meaningfully detect any new biomarkers and assess their clinical importance.

ANNs can therefore be very helpful in the assessment and validation of the biomarkers. For instance, a study indicated that Ki67 is a significant indicator of both illness progression and survival [40]. In order to verify this, Green et al. developed an artificial neural network (ANN) that was intended to validate Ki67 gene expression in relation to another possible DLX2 candidate [19]. The two Ki67 and DLX2 showed significant predictors of future tumors, according to univariate analysis. However, the percentage of patients with elevated levels of Ki67 in prostate cancer is just 6.8%. Thus, this study demonstrated that individuals who qualify for targeted therapy alone might be identified using these two biomarkers [19].

Proteomics can be helpful in alongside the expression of genes in discovering putative biomarkers. For instance, Kim et al. created a unique method to find new possible proteomic markers for prostate cancer by fusing biological computation with targeted proteomics [20]. In a sample of 74 patients, 133 differentially expressed proteins were first assessed using synthetic primers. They then used machine learning techniques to use these candidates to create clinical prediction models. The findings demonstrated the potential of computationally guided proteomics for the identification of new noninvasive biomarkers. The promise of AI ANNs to provide more efficient biomarker selection and validation to support prostate cancer monitoring is demonstrated by a plethora of studies.

### 3.7 ANN in Patient-centered Therapy

Individuals who receive a prostate cancer diagnosis frequently don't know what their alternatives are for therapy. Thus, having a better understanding of how specific therapy are implemented may help patients feel more at ease and satisfied. In order to give patients more control over their care, Auffenberg et al. created a registry that made use of ANN [13]. Data from 46 urology practices that are a part of the Michigan Urological Surgery Improvement Collaborative (MUSIC) are gathered by this registry, askMUSIC. Using the registry data, a random forest ML model is developed that has the potential to forecast prostate cancer therapy alternatives. To allay their fears of a particular therapy, patients can visit the askMUSIC website and engage with the registry's information and projected treatment to display therapy possibilities.

The PRODIGE program by Alitto et al. [11] employs an umbrella protocol that focuses on standardizing data sharing in a comparable setting. Using semi-formal ontology to express clinical variables, a systematic knowledge sharing procedure is established inside this protocol. Both conventional statistics and machine learning can be used with this procedure. The multi-factorial DSS, which serve as the foundation for decisions on patient-level supportive therapy in the future, are supported by the standardization of these methodologies. All things considered, a number of research demonstrate how AI ANNs may be used to create patient-centered technologies that effectively inform patients about available treatments and the advancement or regression of their diseases.

### 3.8 Using ANN to Develop a Prostate Cancer Risk Stratification Classification System

The National Comprehensive Cancer Network (NCNN) criteria for classification of risk now in use rely on the TNM (tumor, node, metastasis) score, Gleason grade, prostate-specific antigen level, and biopsy data [41]. Patients are categorized into risk groups based on these characteristics, which are further divided into seven groups, from extremely low to extremely high. Physicians can help patients choose from a

variety of individualized treatment options, including as radiation, hormone therapy, radical prostatectomy, and active surveillance, based on these risk categories. Although these risk categories provide a useful foundation for classification, none of them consider the possibility of recurrence. Therefore, a deeper comprehension of the mechanisms underlying recurrence could empower us to modify risk variables and, consequently, choose the most appropriate course of treatment.

In order to forecast this recurrence, Kumar et al. built two distinct convolutional neural networks (CNNs) and examined H&E pictures [21]. Individual nuclei were identified by the first CNN, and the patches surrounding the nuclear centers were classified by the second CNN. Patients were asked to vote in order to determine their probability of recurrence. Following 80 case/control pairs for training, Thirty recurrent and thirty non-recurrent controls were used for validation. The precision of the end yield was 0.81 the area under the curve In order to create a new system of scores that may be more precise than the ones in use now, recurrence could be examined in conjunction alongside other risk indicators using a deep learning technology [42].

Apart from recurrence, basic demographics are typically overlooked by the existing methods used to identify indicators of risk for prostate cancer. However, a study by Naguib et al. assessed an integrated method of artificial neural networks (ANN) and conventional statistics that are aware of different risk indicators [23]. In addition to two experimental indicators of the immunostaining for p53 and bcl-2, the neural network used in the present research was developed on conventional parameters such as age, stage, CT scan findings, grade, prostate specific antigen, and treatment. The prediction models only identified patients with the illness with 60% accuracy when traditional risk variables were taken into account. However, after the testing markers were added, this efficiency increased to 80%. As a result, when the volume of data fed into the algorithm increased, the precision of the model improved significantly. This study also emphasized how crucial it is to incorporate experimental markers for testing while creating networks because every piece of information has the potential to significantly affect the correctness of the model. All things considered; several research demonstrate how AI ANNs may be used to create an efficient risk for prostate cancer stratification categorization system.

## 4. CONCLUSION

Artificial intelligence as a tool for managing medical issues has been studied for a while. However, we have only lately been able to make substantial progress due to advances in technology. Artificial intelligence (AI) has the potential to simplify and expedite tasks that are extremely complex and time-consuming for humans, such as managing massive data sets and identifying complex relationships. In addition, a great deal of subjectivity is inherent in the diagnosis and risk categorization that follow to qualify for active surveillance trials. It's feasible to use fewer resources while increasing trial effectiveness and precision overall by utilizing AI algorithms and lowering the subjectivity level.

Recognizing the financial impact of managing localized prostate cancer is also necessary. A total of $45,957 and $188,928 [42] will be spent over ten years managing patients with prostate cancer who are at low and high risk, respectively. However, a more widespread use of AI can undoubtedly aid in lessening this load. AI also makes it possible to achieve this while preserving or even improving the results of ongoing monitoring trials. Thus, to lower costs, enhance results, and propel urologic cancer forward as a whole, we must acknowledge and improve the current pathways. For example, Leeds Teaching Hospitals NHS Trust in the UK has been using a Prostate Intelligence (Pi) Tool, developed in collaboration with Lucida Medical. This analyzes MRI scans to identify prostate cancer lesions and aims to speed up the diagnosis. Similarly, Mount Sinai Hospital in New York, in parternship with PATHOMIQ INC., has created an AI tool called PATHOMIQ_PRAD to improve risk stratification in prostate cancer treatment. There are several such cases where practical use of AI has been revolutionizing diagnosis of the diseases.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declares that generative AI technologies such as Large Language Models, etc have been used during writing or editing of this manuscript. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology.

**Details of the AI usage are given below:**

1. ChatGPT,4, 4o, OpenAI. “Consider yourself as a computer scientist. Fix the grammar and language wherever necessary without changing the original content for conclusion section.

## COMPETING INTERESTS

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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