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Review Article

Artificial Intelligence in Uropathology: Current Applications and Clinical Implementations – A Narrative Review

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Abstract

Artificial Intelligence (AI) has gained increasing popularity as a tool for the histopathological assessment of urological cancers. The aim of this narrative review is to examine current applications of AI, its potential integration into clinical practice, and the challenges associated with its implementation. The publications used for this review were found on PubMed and included relevant English language publications published between 2020 and 2026, with earlier studies being used where necessary for context. This review describes the usage of deep learning and machine learning for various urological cancers such as prostate, renal, bladder and testicular cancers. Current evidence supports the fact that AI can be used as a supportive tool for selected diagnostic and prognostic tasks; however, clinical usage of AI remains challenging due to various factors including dataset shift, inconsistent validation, workflow requirements, regulatory issues, and the lack of prospective evidence demonstrating clinical benefit. Emerging technologies continue to offer further opportunities, with multimodal AI approaches and three-dimensional models, which may extend the prognostic and diagnostic capabilities. Although the use of AI is helpful and supports pathologists, further validation is still needed before a wider clinical adoption.

Keywords: Artificial intelligence; Uropathology; Digital pathology; Histopathology; Whole slide imaging; Machine learning; Deep learning; Convolutional neural networks; Urological cancers; Prostate cancer; Bladder cancer; Urothelial World Health Organization; Renal cell carcinoma; Testicular cancer; Cancer detection; Tumor classification; Tumor grading; Gleason grading; Tumor staging; Tumor segmentation; Tumor quantification; Prognosis; Biochemical recurrence; Lymph node metastasis; Lymphovascular invasion; Immunohistochemistry; Clinical implementation; Workflow integration; Model generalizability; Multimodal artificial intelligence; Three dimensional pathology; Precision oncology

List of Abbreviations: 3D: Three-Dimensional; AI: Artificial Intelligence; AUC: Area Under The Curve; BCR: Biochemical Recurrence; Ccrcc: Clear Cell Renal Cell Carcinoma; CK AE1/3: Cytokeratin AE1 / AE3; Cnns: Convolutional Neural Networks; DL: Deep Learning; GG: Grade Group; H&E: Hematoxylin And Eosin; IHC: Immunohistochemistry; ISUP: International Society Of Urological Pathology; K: Cohen's Kappa (Agreement Coefficient); LVI: Lymphovascular Invasion; ML: Machine Learning; MRI: Magnetic Resonance Imaging; NSGCT: Non-Seminomatous Germ Cell Tumour; Pca: Prostate Cancer; Pccrct: Papillary Clear Cell Renal Cell Tumour; PSA: Prostate-Specific Antigen; RCC: Renal Cell Carcinoma; ROI: Region Of Interest; RP: Radical Prostatectomy; Ta / T1: Non-Invasive Papillary Tumour (Ta) And Tumour Invading The Lamina Propria (T1); Uca: Urothelial Cancer; WHO: World Health Organization; WSI: Whole Slide Imaging / Whole Slide Image(S)

Introduction

The global population has increased substantially over the recent decades [11]. Population aging has been accompanied by an increasing burden on age-related diseases, in particular cancer. Over recent decades, declining cardiovascular mortality in many middle- and high-income countries has coincided with an increasing burden of cancer mortality. Between 2000 and 2015, the standardized mortality rate increased by 7% across countries studied, while cardiovascular disease age-standardized rate decreased over the same period. This rise in cancer patients has resulted in an increase in workload for pathologists; this increase in workload has increased the need for efficient and scalable diagnostic workflows. Beginning from the mid nineteenth century, microscopy subsequently became a fundamental component of pathological examination, enabling the assessment of tissue morphology following appropriate preparation and staining, where a number of steps were carefully performed in order to examine a thin layer of tissue mounted on a flat glass slide, followed by the analysis by staining human tissue with hematoxylin and eosin (H&E) so that scientists can clearly see the different cellular structures.

Recent technological advancements in AI have expanded its potential applications across medicine, particularly in disease detection and diagnosis. AI has been investigated in urology for decades, including its application to prostate cancer detection using prostate-specific antigen (PSA) measurements. Djavan et al. demonstrated the potential of artificial neural networks for early prostate cancer detection in 2002 [37]. In contrast, the application of AI to histopathological image analysis has developed more recently, with ongoing research exploring its potential to support established diagnostic workflows. Pathology represents a field in which AI may support the analysis of complex image-based data and assist established diagnostic workflows. AI-based image analysis may assist with the processing and interpretation of cellular and tissue images, with potential effects on the diagnostic workflow efficiency and consistency. AI refers to computational methods designed to perform tasks that typically require aspects of human cognitive processing, including pattern recognition, prediction and classification. These systems can be trained to identify patterns within data and generate predictions or classifications when applied to new observations. Within AI there are subcategories including machine learning (ML) and deep learning (DL). ML learns to make predictions based on patterns from data while DL is dedicated to using multilayered artificial neural networks to overcome complex tasks.

Within pathology, AI has been investigated for diagnostic, classification and prognostic applications, particularly those involving image-based pattern recognition. A major challenge in prostate cancer (PCa) diagnosis is distinguishing between indolent and clinically significant PCa while reducing unnecessary biopsies and additional diagnostic processes. In a 2003 study, Remzi, Djavan, et al. used an artificial neural network to predict the outcomes of repeat prostate biopsies, reporting a 68% reduction in unnecessary repeat biopsies while maintaining a sensitivity of 95% [38]. These findings suggest that AI may help reduce avoidable invasive procedures and associated healthcare resource use.

Deep learning (DL) algorithms can identify complex patterns within scanned histopathological images, allowing the automated detection and classification of histopathological features. These approaches may support pathologists by facilitating the identification and classification of relevant histopathological features and potentially improving workflow efficiency and diagnostic consistency. Beyond PCa, AI-based approaches have also been able to aid in similar diagnostic and preventive applications in other urological diseases, these approaches have also been investigated in the renal, bladder and testicular tumors.

This narrative review examines current applications of AI in uropathology, with particular focus on the detection, classification, grading, segmentation, and prognostic assessment of urological

cancers. Particular attention is given to prostate, bladder, renal, and testicular tumors, as well as the role of digital pathology and AI-based image analysis. The aim of this narrative review is to evaluate the current evidence regarding the use of AI in uropathological diagnosis, and to discuss its potential integration into clinical practice, including the opportunities and challenges associated with its implementation.

Methods

Search Strategy

This narrative review was conducted using a literature search using PubMed in order to identify relevant studies investigating the use of AI in uropathology and the diagnosis of urological diseases. The search was performed on September 25 2026 using a combination of Boolean terms (AND, OR) and keywords which were related to the topic of AI, prevention, detection, DL, ML, and urological cancers. The search also incorporated terms relating to prostate, bladder, renal and testicular cancers. The complete search string is as follows:

"artificial intelligence"[Title/Abstract] OR "machine learning"[Title/Abstract] OR "deep learning"[Title/Abstract] OR "neural network*"[Title/Abstract] OR "convolutional neural network*"[Title/Abstract] OR "foundation model*"[Title/Abstract] OR "vision transformer*"[Title/Abstract] OR "computational pathology"[Title/Abstract]) AND ("uropathology"[Title/Abstract] OR "genitourinary pathology"[Title/Abstract] OR "prostate cancer"[Title/Abstract] OR "prostate carcinoma"[Title/Abstract] OR "bladder cancer"[Title/Abstract] OR "urothelial carcinoma"[Title/Abstract] OR "renal cell carcinoma"[Title/Abstract] OR "kidney cancer"[Title/Abstract] OR "testicular cancer"[Title/Abstract]) AND ("digital pathology"[Title/Abstract] OR "histopathology"[Title/Abstract] OR "histology"[Title/Abstract] OR "whole slide image*"[Title/Abstract] OR "whole-slide image*"[Title/Abstract] OR "H&E"[Title/Abstract] OR "hematoxylin and eosin"[Title/Abstract]

Eligibility Criteria

The primary literature search was restricted to studies published between 2020 and 2026, written in English. However earlier publications dating from 1995 to 2019 were selectively included when they aided in foundational research or provided essential and historical context relevant to the development of the central idea. The publications used included a range from original research articles, to systematic reviews, meta-analysis and general reviews all of which focused on the core idea of the use of AI in uropathological diagnostic capabilities. Publications were excluded if they were not in English, did not meet the eligible article type criteria or more specifically did not address the scope of the review.

Study Selection and Data Extraction

The initial PubMed Boolean search resulted in 776 records. Applying publication year, language and article type filters removed 661 records, leaving only 115 articles for screening. Following assessment, a further 80 articles were excluded and this resulted in using 35 publications in this narrative review.

The titles were screened by one review in order to ensure relevance which was then followed by a more thorough full-text assessment of the material and checking of plausible material that can be used for the narrative. The selected literature was combined and reviewed in order to have findings from different studies and then were discussed. The studies chosen for the detailed narrative discussion were chosen based on their relevance to review objectives, and findings (Figure 1).

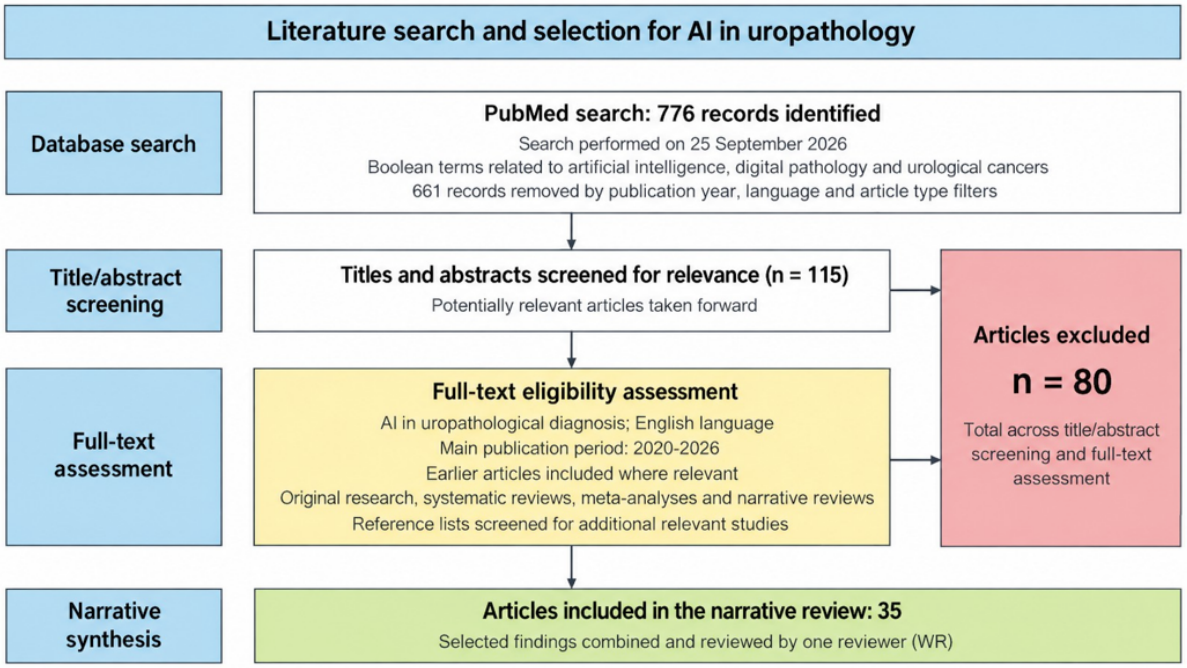

Figure 1: Literature search and selection process

Limitations

The restriction of the search to PubMed by limiting the years of study may have resulted in the omission of several publications, which were indexed in other databases. Furthermore, the approach of applying several filters on publication year, language and article type may have also excluded relevant studies. As this is a narrative review, the selection of studies may be subject to selection bias, as some relevant publications may have been overlooked or excluded during the process

Artificial Intelligence and Digital Pathology

Digital Pathology and Whole Slide Imaging

Digital pathology is the process of digitalizing the information on a glass slide using a Whole Slide Imaging (WSI) scanner by capturing the entire slide of what is seen in the microscope in order to have an electronic image. Once an image is created, a digital examination is made using an image viewer, which is a computational program that can store various graphical images in a database to be looked at and analyzed [7]. Advances in digital pathology have increased the feasibility of integrating WSI into pathology workflows, enabling the examination of a collection of pathological images more efficiently and precisely [5]. Scanners can scan slides in up to 30 seconds [6] while also allowing the pathologist to modify the brightness, contrast and opacity of the slide. In terms of storage, WSI systems are capable of storing up to 1000 slides at a time [6], switching between slide images instantly. The increasing availability of digital pathology infrastructure has facilitated the development and evaluation of AI-based pathology applications.

AI Technologies

AI encompasses several approaches, including ML and DL. ML is considered to be the more traditional approach in which the model learns patterns from previously provided data and subsequently makes inferences and decisions about the new data it is given [8]. Its main premise is that once a model's performance has been optimized on a specific dataset, it can apply the patterns it has learned to real-world problems and make predictions when presented with new, previously unseen data. [8] DL on the other hand is a more complex subset of ML that uses multi-layered neural networks inspired by the interconnected structure of neurons in the human brain. DL models use multiple layers of artificial neural networks to progressively extract increasingly complex features from input data, with each layer performing a mathematical computation and progressively extracting complex characteristics as opposed to ML, which relies more heavily on predefined patterns and recognition mechanisms of mathematical algorithms.

AI Workflow in Pathology

Digitalization may be able to support laboratory workflow by identifying atypical cases that require additional immunohistochemistry (IHC) staining, which can then be performed before the scanned image is reviewed by a pathologist. In addition, this enables quality control and the classification of scans that require re-scanning in order to improve their quality (Figure 2).

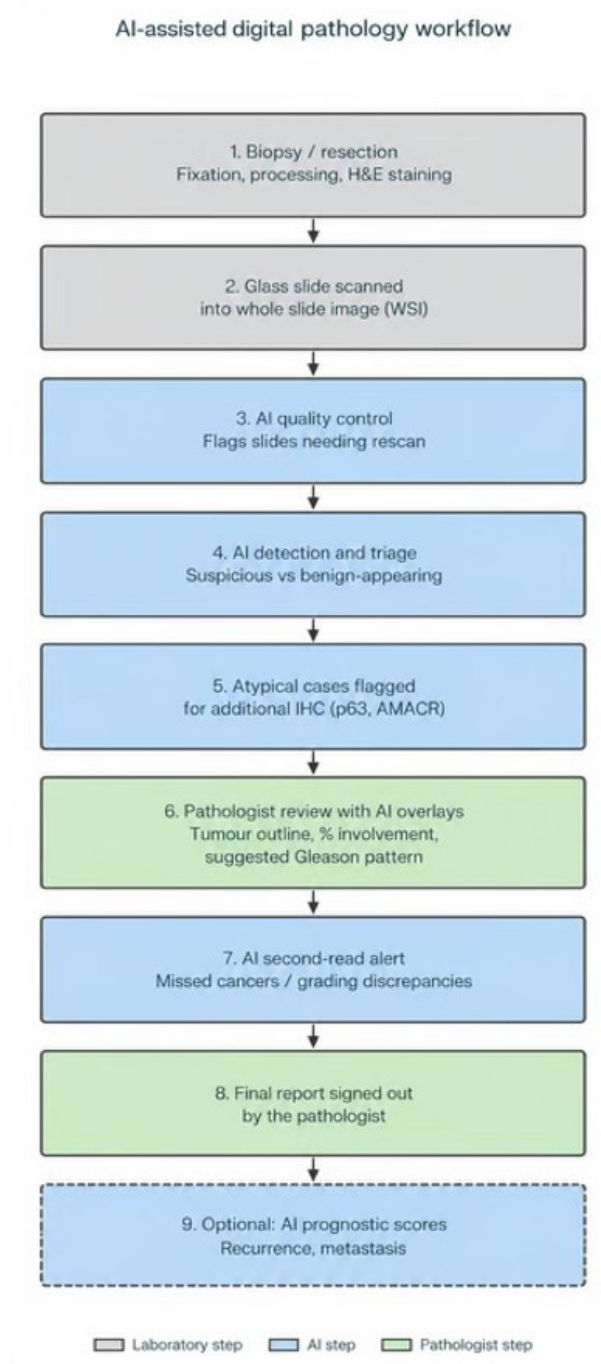

Figure 2: AI-assisted digital pathology workflow in uropathology (Figure created by the author based on ideas from Pantanowitz et al.)

AI Applications in Uropathology

Prostate Cancer

PCa represents one of the most commonly diagnosed malignancies in men and represents an important area of urological practice. With 1 in 8 men being affected by this illness in the U.S. during their lifetime, advancement for screening, diagnosis, and prevention still remains a challenge. These challenges have contributed to increasing interest in digital technologies and AI-based approaches to PCa diagnosis. The final diagnosis of PCa relies on the histopathological examination of prostate tissue obtained through a biopsy. This aids in distinguishing between benign and malignant prostate tissue. However, biopsy interpretation has several limitations including tumor heterogeneity, sampling limitations, sampling contamination and variability in terms of Gleason grading [9]. Although there is a standardized way of analyzing prostate biopsies, with a number of biomarkers and diagnostic criteria, diagnostic interpretation may remain challenging for clinicians, particularly in cases with overlapping morphological features, as there are cases where benign lesions may mimic carcinomas, leading to a complicated diagnosis and grading. Another major challenge is the ability to differentiate between benign and malignant prostate tissue. Examples include atypical adenomatous hyperplasia, atrophy and basal cell hyperplasia [9]. Various IHC markers such as p63, high-molecular-weight cytokeratin and alpha-methylacyl-CoA racemase may assist in diagnostically challenging cases, however, interpretation may still be difficult in cases of limited and fragmented biopsy samples (Table 1).

Study	Study Purpose	Material	What was measured	Results	Conclusion
Lucas et al., 2019 [13]	DL ability to differentiate between higher and lower Gleason patterns in prostate biopsies was examined in this study.	Digital histopathology slides of prostate biopsies was used in the study.	The histological patterns were analyzed from low to high Gleason scores. Their performance was then evaluated using the AUC.	The model achieved an AUC of 0.90 in distinguishing between a Gleason pattern of ≥ 4 and ≤ 3.	The results showed that DL can distinguish relevant Gleason patterns.
Källén et al., 2016 [14]	AI's ability in recognizing and classifying different Gleason patterns was looked at in this study.	There were 213 histopathologic al images of prostate tissue used.	The Gleason patterns were automatically classified and compared with other reference classifications.	A classification accuracy of 81 to 89% was reported.	The study showed that AI detection of Gleason patterns could potentially support PCa grading.
Arvaniti et al., 2018 [15]	AI's ability in achieving a level of agreement similar to that of pathologists in terms of recognizing Gleason scores was investigated in this study.	There was a cohort of 641 patients and an independent cohort of 245 patients. H&E stained microarrays of PCa tissue were used for analysis.	The Gleason patterns assigned by the AI system were compared with the pathologists scores using κ.	The agreement between the AI and the pathologists were $\kappa = 0.75$ and 0.71 respectively.. The agreement among the pathologists was $\kappa = 0.71$.	The agreement between the AI and the pathologists suggested that automated grading could help improve consistency in Gleason scoring.
Vazzano et al., 2023 [16]	The study examined the effectiveness of AI's assistance in PCa detection in several laboratories using different WSI scanners.	There were 30 prostate biopsy samples from two laboratories that were scanned using three WSI scanners, resulting in 90 digital scans.	Cancer foci were detected and tumor size was quantified. Detection performance and agreement with pathologists' assessments were evaluated.	The sensitivity for cancer foci that were < 1 mm was 100%. The AI estimate of tumor quantification also showed a high degree of agreement.	The results suggest that AI could be useful not only for the detection of PCa but also for the localization and quantification of small tumor areas.

Lee et al., 2014 [18]	The study investigated whether quantitative histological features could predict BCR following RP.	There were 40 patients with intermediate risk PCa including patients with and without BCR.	Glandular morphology and the associated glandular angularity were analyzed to distinguish recurrent from non-recurrent disease.	The model achieved an accuracy of 73% in predicting BCR. Cancerous areas could also be differentiated from normal tissue with high accuracy.	The study suggests that quantitative histological features can provide prognostic information in addition to identifying malignant tissue.
Note: AI, artificial intelligence; AUC, area under the curve; BCR, biochemical recurrence; DL, deep learning; H&E, hematoxylin and eosin; PCa, prostate cancer; WSI, whole slide imaging; κ, Cohen's kappa coefficient (agreement between raters); RP, radical prostatectomy.					

Table 1: Summary of studies evaluating AI in Prostate Cancer.

Cancer Detection

A fundamental step in the diagnosis of PCa is the histopathological examination of prostate tissue, which can now be digitalized using WSI. WSI has improved in the efficiency of identifying various pathological abnormalities. The question remains, however, whether the use of AI may aid in the ability to distinguish benign prostate tissue from malignant prostate tissue. AI-based methods, particularly DL approaches such as convolutional neural networks (CNNs), have been investigated for the automated detection and classification of histopathological features, something which can also be used in the prevention and detection of cancer in biopsy samples. DL, particularly through CNNs has shown potential for distinguishing between various histological features. Having been trained using large datasets of prostate biopsies, these models are better able to distinguish malignant from benign tissue; several studies have reported high sensitivity and specificity for cancer detection, with some findings also comparing AI performance with that of expert pathologists. [9]. Morozov, et al. conducted a systematic review, where 24 studies were conducted between 2007 and 2021 overall containing 8000 prostate biopsy cases and 458 radical prostatectomy (RP) cases providing evidence across multiple independent studies. Across the included studies, AI was able to detect cancer between 87-100% across all the studies and detect benign tissue between 68-99% of cases [32]. Overall diagnostic accuracy ranged from 83.7% to 98.3% with the area under the curve (AUC) reaching 0.99. When the studies were statistically combined, the pooled sensitivity and specificity were approximately 96% [32]. These pooled estimates indicate a high diagnostic performance across the included studies to discriminate between malignant and benign prostate tissue. In a different study, Salvi et al., (2023) [10] analyzed prostate tissue stained with various proteins used as IHC markers. These markers were used to facilitate the distinction between malignant and benign prostate glands for the pathologists, while at the same time training the AI systems with new annotations that were not used before. AI was then used to determine whether the different prostate gland types could be successfully identified and classified based on these staining patterns. As a result, the model achieved a Dice score of 90.36%, which demonstrated a high degree of overlap between the tissue regions identified by AI and the reference annotations marked by the pathologist.

In addition to its potential diagnostic applications, the use of AI may also provide clinical benefits such as more efficient biopsy review as well as improving diagnostic reproducibility. AI may also help identify more suspicious or atypical cases that require additional review by a pathologist. Therefore, the use of AI in the diagnosis of PCa may be used as a triage and decision-support tool for pathologists helping to identify and flag cases, which require additional attention.

Gleason Grading

Following histological detection of PCa, assessment of tumor grade is an important component of pathological evaluation. The Gleason grading system is a key component of PCa assessment. It is a grading system used to show the aggressiveness of PCa under a microscope determined by the architecture and characteristics of the glands [12]. It is performed by pathologists who examine prostate tissue and evaluate the patterns of malignant glands. This is then graded on a scale from 6 to 10, where the lower the number on the scale, the more closely the glandular architecture resembles normal tissue. In order to simplify the reading of the Gleason scores both for doctors and the patients, the International Society of Urological Pathology (ISUP) introduced a new way of scoring. This new system ranged from Grade Group (GG) 1 to GG 5, where the lower the number the lower the aggressiveness of the cancer. Multiple parts of the PCa may have different grades; therefore pathologists tend to grade the predominant and secondary Gleason patterns [12]. Once the two Gleason patterns are identified, their sum determines the Gleason score, which is then converted into the ISUP grading system: Gleason 6 (3 + 3) (ISUP 1), Gleason

7 (3 + 4) (ISUP 2), Gleason 7 (4 + 3) (ISUP 3), Gleason 8 (4 + 4) or (3 + 5) or (5 + 3) (ISUP 4), and Gleason 9 and 10 (ISUP 5) [1]. This score remains to this day one of the most important determinants of PCa risk, prognosis and treatment selection [9]. However, assessment of Gleason patterns can present diagnostic challenges. The first of which is the difficulty in distinguishing between Gleason patterns particularly patterns 3 and 4 and 9 and 10. In these cases, the expert pathologist would need to use their experience to interpret the results. This may contribute to interobserver variability in grading. To address these challenges, AI systems have been developed in order to be able to grade various PCa tissues based on this Gleason grading system. This was done using DL systems where the AI interface was trained on annotated histopathological datasets. Several studies were conducted to explore whether the AI was effective for PCa grading. Studies using AI conducted by Lucas et al reported an AUC of 0.90 for differentiating Gleason grade ≥4 from ≤3. In another study by Källén et al. the AI system achieved an accuracy of 81% to 89% in classifying Gleason patterns [14]. When compared with expert pathologists' score, Aravanti et al used a cohort of 641 patients of whom 245 patients had pathological samples annotated by pathologists. This then measured an agreement using Cohen's quadratic kappa (κ) between AI-based Gleason grading and pathologist assessment, with agreement coefficients of 0.75 and 0.71. This suggests that the agreement of analysis between AI and pathologists was substantial. Leite et al conducted a study using DL for an AI interface using 1525 pathological images from 12 slides of RP specimens. The AI system was able to distinguish between benign tissue and Gleason patterns 3, 4, and 5 achieving an accuracy of 96.7%, 92.5%, 96.5%, 76.6% respectively, resulting in an average precision of 91.2% [9]. Collectively, these studies suggest that AI-assisted grading can achieve substantial agreement with pathologist assessment in selected databases, suggesting that the use of AI may improve grading consistency, reproducibility and accuracy.

Tumor Segmentation and Quantification

AI-based image analysis may also assist with tumor segmentation, which is the outlining of where the tumor is on the slide and automatic quantification of its dimensions. With the use of DL, AI models can be trained to take these measurements automatically, potentially reducing the need for manual delineation. In a study done by Vazzano et al, an AI system called INIFY Prostate (an AI-based software designed to analyze and outline cancer areas in prostate biopsy samples, was used on 30 prostate biopsy specimens from two different laboratories in the United States. In this sample, 20 biopsies were PCa and 10 were benign, and all of them had different Gleason scores. The biopsy samples were then scanned using three different WSI in order to induce variation to the data and test the robustness of the AI algorithm. The 90 digital scans were then given to the INIFY Prostate system, which flagged two characteristics; first was the segmentation part, which was being able to identify suspicious cancer, and second was the quantification aspect of it; how much of the biopsy was occupied in this suspicious area that it flagged. As a result, the correlation between the percentage of suspicious areas of cancer which was determined by the AI algorithm and the percentage of cancer length estimated by human pathologists' findings was very strong, with a regression coefficient of 0.76-0.80 [16]. The system also detected very small tumor areas, including lesions measuring less than 1 mm with a sensitivity of 100%. In one of the prostate samples which was considered to be a GG 1 grade cancer with a length of 0.3 mm (representing 1.8% of the biopsy length), the AI system predicted the suspicious cancer area of being 1% of the biopsy length, proving the close approximation between AI systems and humans in quantification of cancers.

Prognosis

Prognosis refers to the expected clinical course and outcome of a disease [17]. After urological procedures such as a RP, the pathological report is very important in order to determine a patient's prognosis. This may establish the likelihood of biochemical recurrence (BCR) and inform the most appropriate treatment options. AI may also aid in the prognostication through its ability to analyze histopathological images and recognize various morphological features that may suggest recurrence. Such information may support risk stratification and treatment planning. Johns Hopkins University trained an AI model using DL methods to analyze PCa tissue images from various tissue microarray spots, 72% of which were derived from recurrence cases. The AI model was able to demonstrate PCa recurrence resulting in an odds ratio of 3.28 per unit increase in the AI-derived biomarker [1]. The model was then further tested after adjustment for ISUP grade, PSA level, and year of prostatectomy, and even then it maintained a strong association. These findings further suggest that AI-derived morphological features may provide additional prognostic information for the assessment of PCa recurrence. Huang et al used an AI model's morphological scoring system to identify certain regions of interest (ROI) which were associated with cancer recurrence. The study further showed that high expression of TMEM173 (an immune-related gene) may represent a useful biomarker associated with PCa recurrence, suggesting that AI-based analysis may assist in predicting recurrence, further demonstrating the potential of AI in predicting cancer recurrence. Because PCa can vary in biological aggressiveness, assessment of tumor characteristics can provide important information for prognostic evaluation. In a study conducted by Lee et al an AI model was trained using digitized histopathological images to differentiate between high-risk PCa and low- to intermediate-risk cancer. Traditionally, aggressive risk cancer has greater

architectural disorganization of the glands compared to low risk cancer and therefore the level of disorder related to the glandular angularity features were higher in aggressive cases and lower in low risk cases [3]. In this study, 40 intermediate risk PCa patients who underwent RP were used, half of which experienced BCR. 56 different cancer regions of the prostate were annotated across the 40 patients; 28 from patients with BCR and 28 from patients without recurrence [18]. The study evaluated whether the AI model could distinguish between patients who experienced PCa recurrence, those who did not based on tumor appearance, and glandular angularity features. The AI model achieved an accuracy of 73% and out of the 80 ROI; the model was able to have a 99% accuracy in distinguishing regions containing PCa from normal tissue. AI algorithms have also been trained not only to predict recurrence but also for other critical outcomes such as metastasis [3]. A study used CNNs in order to predict lymph node metastasis around the area where the PCa was removed, just by looking at histopathological images. The CNNs trained on these biopsy images achieved a mean AUC of 0.68 and a balanced accuracy of 61.37%, indicating potential utility for predicting lymph node metastasis [3]. This study shows that the use of CNNs may be useful as a low cost method for extracting important prognostic information from images in order to determine metastasis to sites such as the lymph nodes in PCa patients.

Bladder and Urothelial Cancer

Bladder cancer is the 10th most diagnosed cancer worldwide, with over 614,000 new cases estimated globally [19]. AI-based systems have been investigated for the detection, grading, and classification of histopathological features in bladder and urothelial cancer (UCa). Detection of cancers is a critical component of diagnosis. AI systems can be used to distinguish normal from UCa, potentially improving diagnostic accuracy. Zhang et al developed an algorithm to diagnose papillary UCa. In their study, they used 913 WSI from patients with bladder cancer. Two human pathologists annotated tumour and normal tissue regions. After having the AI system review the images, it successfully had a positive rate of 0.95 in discriminating between normal and tumor tissue [33]. Similarly, Noorbakhsh, et al. performed a similar study where the AI model achieved an AUC of 0.98 in distinguishing between normal and tumor tissue. These findings indicate that AI-based image analysis may distinguish normal from tumor tissue in the investigated datasets [34]. When it comes to grading UCa, AI models have shown promising performance. Jansen et al performed a study using 328 transurethral resections of bladder UCa [35]. The model was able to successfully distinguish between low and high grade UCa, correctly grading 76% of the low grade and 71% of the high-grade cases [35]. When comparing the results of the model to that of human pathologists, it was seen to have a moderate level of agreement, with a κ value of 0.48. Although this represents only moderate agreement, when compared to the level of agreement between three other human pathologists, which showed a κ value of 0.35, 0.38 and 0.52 respectively, these findings suggest that the use of AI specifically in grading of UCa may improve grading consistency. When it comes to seeing whether various AI models are able to differentiate tumor stage or depth of invasion. Yin et al conducted a study where they trained an AI model in order to be able to analyze the shape, size and colour of the nucleus and cytoplasm. 1,177 stained bladder tumor images were taken, of which 460 were non-invasive Ta (tumor has not invaded the lamina propria) tumors and 717 were T1 (tumor has invaded the lamina propria but not the muscularis propria) tumors [7]. The AI analyzed various morphological features and characteristics. Six models were able to differentiate Ta from T1 tumors with accuracies ranging from 91% to 96% [7]. These findings indicate that AI models may distinguish between selected tumor categories with high accuracy in the investigated datasets. In addition to cancer detection, accurate assessment of invasive growth patterns may provide clinically relevant prognostic information. Garcia et al tested the efficacy of an AI system in detecting invasive patterns [20]. This study focused on muscle invasive bladder cancer, which is known to have a poorer prognosis, and greater potential to metastasize beyond the bladder. The tissue was stained with Cytokeratin AE1 / AE3 immunohistochemistry, which was able to highlight viable tumor cells. The AI system identified tissues that were not cancer related, mild and infiltrative patterns and was able to group the cells in these categories. Not only was the model unsupervised, but it achieved an average multiclass accuracy of 90.34%, indicating that AI-based analysis may provide additional information relevant to prognostic assessment and clinical decision-making (Table 2).

Study	Study Purpose	Material	What was measured	Results	Conclusion
Zhang et al., 2024 [33]	AI's ability in detecting UCa when given digital histopathological specimens.	WSI of bladder cancer tissue, with pathologists labeling tumor and normal areas.	Tumor tissue from normal urothelial tissue was measured by analyzing the histological regions.	For the identification of the tumour, a true positive rate of 0.95 was found.	The results suggest that AI can support the automated detection of UCa, although the findings pertain to the specific tumor morphology considered in the study.
Noorbakhsh et al., 2020 [34]	DL's ability in differentiating between tumor tissue and normal tissue when given various cancer types.	There were 27,815 H&E stained WSIs from the Cancer Genome Atlas. They covered 19 solid tumor types including bladder cancer.	CNNs were used for the classification of tumors compared to normal tissue as well as for other histopathological prediction tasks across various cancer types.	This resulted in an AUC value of 0.98, the tumor vs normal tissue classification performed well across all cancer types that were investigated.	The study showed that DL can distinguish between tumor tissue and normal tissue in various types of cancer, demonstrating its potential use in histopathological cancer detection.
Jansen et al., 2020 [35]	Developing an automated system for identifying and grading UCa that is not muscle invasive.	There were 328 transurethral resections of bladder UCa used.	The system identified urothelium and classified tumors as low or high grade. AI grading was compared with expert pathologist consensus.	The model graded 76% of low-grade and 71% of high-grade cancers. Agreement with pathologist consensus was $\kappa = 0.48 \pm 0.14$.	Agreement between AI and experts' evaluations was moderate, suggesting that the system might be useful as a supportive tool rather than as a standalone evaluation method.
Yin et al., 2020 [7]	To investigate whether ML could distinguish non-invasive Ta from invasive T1 bladder tumors.	1,177 H&E-stained images, including 460 Ta and 717 T1 images.	Morphological features of the nuclei, cytoplasm and surrounding tissue were extracted and used to classify Ta and T1 tumors.	Six supervised ML methods achieved 91–96% accuracy, while CNN-based automatic feature extraction achieved approximately 84% accuracy.	The study showed that pathology-based morphological features can be useful for distinguishing Ta from T1 disease and may assist in assessing tumor invasion.
Garcia et al., 2021 [20]	To investigate the ability of an AI System to detect different invasive patterns.	Bladder cancer tissue stained immunohistochemically with CK AE1/3.	Tumor regions and histological growth patterns were classified into different morphological categories.	The model achieved an average multiclass accuracy of approximately 90.34%.	Automated analysis of tumor growth patterns could provide additional information to support the pathological assessment of invasive bladder cancer.

Note: AI, artificial intelligence; UCa, urothelial cancer; WSI, whole slide image; H&E, hematoxylin and eosin; CNN, convolutional neural network; AUC, area under the curve; DL, deep learning; κ, Cohen's kappa coefficient; ML, machine learning; Ta/T1, non-invasive papillary tumor (Ta) and tumor invading the lamina propria (T1); CK AE1/3, cytokeratin AE1/3.

Table 2: Summary of studies evaluating AI in Bladder and Urothelial Cancer.

Renal Tumors

Renal cell carcinomas (RCC) are characterized by histopathological features, which are essential for diagnosis and treatment planning. Accurate classification of RCC is clinically relevant because their biological behavior and prognosis vary substantially between tumor subtypes and grades. An application of AI in this field is the differentiation between papillary clear cell renal cell tumor (pccRCT) which has low potential and distinguish it from clear cell renal cell carcinoma (ccRCC) which is a malignant RCC subtype with aggressive behavior. Adeltawab, et al. developed a learning framework consisting of three CNNs in order to analyze WSI of renal tissue. The study included 64 WSI images classified into four different categories. The AI system's task was to analyze the images at three different magnifications and be able to generate an image map where each pixel is classified into one class [21]. The model successfully distinguished pccRCT from ccRCC achieving an accuracy of 91%. For RCC, there are two main grading systems; World Health Organisation (WHO) / ISUP systems and the Fuhrman grade. The distinction between the two systems is that the WHO/ISUP system places greater emphasis on nuclear prominence whereas the Fuhrman system incorporates nuclear size, shape and nuclear prominence. Similar to the study done by Lucas et al in training an AI system to differentiate between Gleason scores that were ≥4 from ≤3, Yeh et al trained an AI model to distinguish between low grade and high grade RCC. This distinction is clinically relevant because differentiation between low-grade (Fuhrman grades 1–2) and high-grade (Fuhrman grades 3–4) tumors may inform prognostic assessment and treatment planning [25]. The study successfully achieved an AUC of 0.97, indicating high discriminatory performance (Table 3).

Study	Study Purpose	Material	What was measured	Results	Conclusion
Abdelta wab et al., 2022 [21]	Analysis of a DL approach for kidney tumour histopathology classification that is automated.	There were 64 WSI used of which they were divided into four histopathological categories.	Three CNNs produced classification maps for the different tissue categories after analyzing kidney tissue at different magnifications.	The framework's classification accuracy was approximately 91%.	The results show that DL can be used on multiple scales for the classification of kidney tumors, although the relatively small dataset limits conclusions regarding broader clinical application.
Yeh et al., 2014 [25]	Finding out whether quantitative nuclear characteristics are able to differentiate between ccRCC of low and high grade.	Digitized histopathological images of ccRCC.	The nuclear features were measured using computer-aided analysis and used to distinguish between low- and high-grade tumors.	The method achieved an AUC value of approximately 0.97 in distinguishing between low- and high-grade ccRCC.	The quantitative assessment of nuclear morphology demonstrated high discriminatory power and could potentially support a more objective grading of ccRCC.

Note: WSI, whole slide image; ccRCC, clear cell renal cell carcinoma; CNN, convolutional neural network; AUC, area under the curve; DL, deep learning.

Table 3: Summary of studies evaluating AI in Renal tumors.

Testicular Tumors

Testicular cancer is the most common cancer in young males aged 15 to 35 [23]. Histopathological assessment plays a major role in determining the type of testicular tumors and identifying its various characteristics that may influence their staging and prognosis. For example, features such as lymphovascular invasion (LVI) and the presence of embryonal carcinoma may provide critical information for disease progression and prognosis. Although AI applications in testicular pathology remain less extensively studied than those in other areas of uropathology, several studies have investigated the use of AI to identify histopathological features relevant to the diagnosis and prognosis of testicular tumors. The detection of LVI refers to the presence of tumors that present within endothelial-lined lymphatic or vascular channels [22]. LVI is considered to be an important prognostic marker in testicular germ cell tumors. Assessments of a large number of slides for LVI can be time-consuming for pathologists. Ghosh et al performed a study whose aim was to assess whether the use of an AI algorithm was able to identify ROI that were suspicious for LVI. The system was given a database consisting of 104 WSI from 9 patients with testicular germ cell tumors [22]. The dataset included both seminomatous and non-seminomatous cases. The AI model was further trained to classify and identify the various areas that were suspicious for LVI. The model was able to identify 34 foci across the 104 WSI leading to a precision of 0.68 for identifying areas considered appropriate to flag possible LVI. Three different human pathologists then evaluated these areas. Although the AI system was successful in identifying areas suspicious for LVI, there were some false-positive regions, which included embryonal carcinoma in the tunica albuginea and rete epithelium. Beyond the detection of LVI, AI has also been trained to combine histopathological features in order to be able to predict the pathological stage in testicular cancer. Moul et al investigated 93 patients with clinical stage I Non-Seminomatous Germ Cell Tumors (NSGCT) [24]. The main issue with NSGCT is that some patients may have occult metastatic disease, which is not apparent during the initial clinical staging process. Therefore, the study was performed to see whether characteristics of the primary testicular tumor could help predict the pathological stage of the patient using two important histological characteristics; primary tumor vascular invasion and percentage of the tumor composed of embryonal carcinoma. The conventional statistical model correctly predicted the pathological stage in 86% of patients. The same database was given to a neural network AI model, where it correctly predicted the pathological stage in 92% of patients [24]. These findings suggest that AI-based models may assist in the identification of histopathological features relevant to pathological staging in patients with testicular cancer (Table 4).

Study	Study Purpose	Material	What was measured	Results	Conclusion
Ghosh et al., 2021 [22]	AI's ability in detecting regions in testicular germ cell cancers that are suggestive of LVI.	The validation set included 118 WSI's from 10 patients and 184 H&E Stained WSI's from 19 patients.	The algorithm identified areas suspected of LVI, which were later reviewed by pathologists.	The model identified 34 suspicious areas. The precision was 0.68 for areas where the labeling was considered appropriate and 0.56 for areas where definitive LVI was present.	The results suggest that AI could be used to flag suspicious areas for further review, but the occurrence of false positive findings means that assessment by a pathologist remains necessary.
Moul et al., 1995 [24]	The quantitative capability of neural networks in predicting pathological stage in clinical stage I NSGCT.	There were 93 patients with clinical stage I NSGCT.	In order to predict the pathological stage, there were various histological characteristics such as vascular, lymphatic, and tunical invasion were examined along with the percentages of teratomas, seminoma, yolk sac cancer and embryonal carcinoma.	The neural network correctly classified 86 of 93 patients resulting in a 92% accuracy, with a sensitivity of 88% and a specificity of 96%.	The study showed that combining multiple quantitative histological features in a neural network could help predict the pathological stage.

Note: AI, artificial intelligence; LVI, lymphovascular invasion; H&E, hematoxylin and eosin; WSI, whole slide image.

Table 4: Summary of studies evaluating AI in Testicular tumors.

Clinical Implementation, Challenges and Limitations

Pathologist–AI Collaboration and Workflow Integration

The integration of AI has demonstrated benefits in multiple ways when used in clinical pathology. Studies discussed previously demonstrate the potential of AI and how it may be incorporated at different stages of uropathological workflow including detection, grading, segmentation, quantification and prognosis. One example is the study conducted by Vazzano et al, which incorporated an AI system called INIFY Prostate. This system was able to flag areas of interest that had suspicious cancer and also was able to quantify how much of the biopsy was occupied by the cancer. Human pathologists performed the same assessment and when comparing results, a regression coefficient of 0.76-0.80 was found between humans and the AI model. This demonstrates the degree of agreement between AI and human assessment. These systems may be incorporated as they can be integrated into workflow pathology even as an initial screening tool or triage tool where WSIs are first analyzed by AI systems with suspicious cases subsequently reviewed by human pathologists. An example of such a workflow is summarized in Figure 2. Pantanowitz et al demonstrated this by using AI as a second research tool in routine clinical practice. The algorithm reviewed 11,429 prostate biopsy slides and generated alerts for where cancers may have been missed as well as detected potential discrepancies in Gleason gradings that may have been initially missed by the pathologist [27]. This may reduce review time and may also allow pathologists to allocate greater attention to cases requiring greater diagnostic attention, as well as acting as a safeguard against potentially missed findings. Eloy et al found that with the implementation of AI, pathologists can reduce the need for IHC and second opinions while at the same time maintaining accuracy [36]. The same thing can be done with PCa grading, as similar studies have seen a substantial agreement between human pathologists and AI models [9,14]. One study showed that the use of AI increased the sensitivity for detecting PCa smaller than 0.6mm from 46% to 83% [5,26], suggesting that AI may provide an additional assessment which may support grading reproducibility and consistency.

Challenges to clinical implementation

Having analyzed various clinical studies demonstrating the potential clinical benefits of AI, there are, however, some limitations in terms of its generalizability to images generated by different protocols or samples from different populations [2] When AI algorithms are trained on datasets from a specific population, they are thoroughly trained and are able to recognize the recurring patterns in that cohort. However, when it comes to dataset heterogeneity, including staining variations, artefacts and imaging differences between scanners, the AI models perform less effectively, ultimately limiting their widespread use [5]. To address this issue, large and diverse training datasets are required, so that the algorithm can include a broad range of cases collected over extended periods from multiple institutions and clinics to improve generalizability to real-world target populations. Not only is heterogeneity a limitation in AI but also its difficulty in tackling rare conditions such as atypical acinar proliferation, atypical intraductal proliferation, another diagnostically challenging histological subtype [5]. This is because during its training, rare conditions may be underrepresented in AI training datasets, therefore posing challenges when faced with real world scenarios. Anagnostou, Djavan, et al. highlighted several challenges associated with the clinical implementation of artificial neural networks, including medical record quality, precautions in their use, resistance to adopting these systems, and the need for common standards to support their integration into clinical practice [39]. When it comes to legal and ethical considerations, it is unlikely that the use of AI will fully replace human pathologists in the near future. Despite demonstrating promising performance and accuracy, there will still need to be a human pathologist to review the work of the algorithm and use its human judgment in certain scenarios.

Future Directions

Emerging AI technologies

In addition to using AI systems in diagnosis, grading and prognostication of various urological diseases, emerging technologies are creating new possibilities for assessment of urological diseases such as cancer. One example is TriPath, which addresses a limitation of conventional pathology. Human tissue was traditionally examined through histopathological examination as a limited two-dimensional cross-section, and therefore they aimed to enable three-dimensional visualization [28]. Their study demonstrated that by seeing these images as three-dimensional (3D), prognostic performance for PCa improved, achieving an AUC of 0.804 compared with 0.744 for the clinical baseline [28]. In addition, another application of AI is for PCa detection on magnetic resonance imaging (MRI). This investigated whether the use of AI systems can potentially aid in the diagnostic pathway of PCa by analyzing MRI images directly as opposed to histopathological scans. It was seen that AI produced 50.4% fewer false positive results and 20% fewer detections of Grade 1 Gleason group cancers. These findings suggest that there are a number of other ways the use of AI can support a primary PCa diagnosis.

Multimodal AI and precision Urological Oncology

Another important future direction for urology in terms of the development of technology particularly AI is the advancement of multimodal AI. This refers to the integration of multiple data modalities of AI systems where different forms of patient

information can be combined to provide more personalized diagnostic and treatment guidance. Chen et al developed a multimodal AI model, which combined histopathological images with genomic information in order to predict survival outcomes [29]. This study was done on ccRCC and demonstrated improved prognostic performance compared to other models, which used a single data modality. Another study investigated PCa, where WSI of PCa biopsies were combined with clinical variables such as age, PSA levels and Gleason grade in order to predict the benefit of androgen deprivation therapy [30]. Both of these studies highlight the potential of AI, more specifically in multimodal systems, which may allow uro oncology to move beyond the analysis of a single data modality, and thus integrate multiple data types including clinical information in order to improve diagnostic assessment and support more personalized treatment planning. Beyond just multimodal approaches, another emerging direction is the development of models capable of performing multiple pathological tasks across different cancer types. One example is the Clinical Histopathology Imaging Evaluation Foundation, which developed a model by scientists at Harvard Medical School for the explicit purpose of digital pathology and cancer risk assessment. This model has been used to perform diagnostics across 19 different types of cancers and it successfully was able to have a 94% accuracy in cancer detection across multiple databases from where it collected information. This broader capability demonstrates the potential of models to move pathology beyond highly specialized single-task systems and move towards more generalizable platforms.

Conclusion

AI has demonstrated potential across multiple areas of uropathology, including cancer detection, histopathological classification, Gleason grading, tumor segmentation, quantification, and prognostic assessment. Applications have been investigated in prostate, bladder, renal, and testicular tumors, with studies reporting high diagnostic performance in several specific tasks and datasets. However, the level of evidence and degree of clinical validation vary between applications.

Despite these findings, several limitations remain before AI-based systems can be routinely integrated into clinical practice. Models trained on specific and relatively homogeneous datasets may demonstrate high performance on similar cases but may perform less effectively when applied to heterogeneous or atypical cases. Other challenges include limited external validation, differences in patient populations and laboratory workflows, underrepresentation of rare pathological entities, regulatory requirements, implementation costs, and data governance. Importantly, high diagnostic performance in retrospective or selected datasets does not necessarily translate into improved patient outcomes or cost-effective implementation in routine clinical practice.

The future role of AI in uropathology should therefore be considered primarily as an adjunct to professional expertise rather than as a replacement for pathologists. AI-based systems may assist with repetitive and time-consuming tasks, highlight suspicious areas, support grading and quantification, and help prioritize cases requiring detailed human assessment. Such applications may allow pathologists to use their expertise more efficiently while maintaining responsibility for the final interpretation of pathological findings and their integration with clinical information.

Further prospective, multicentre studies and independent external validation are required to establish the clinical utility, safety, generalizability, and cost-effectiveness of AI-based diagnostic systems. Emerging approaches, including three-dimensional pathology and multimodal AI, may further expand the applications of AI in uropathology. Ultimately, successful integration of AI into clinical practice will depend not only on improvements in algorithmic performance, but also on appropriate legal frameworks based on local governance, effective workflow integration, and finally the continued collaboration between clinicians and the AI systems, as well as healthcare professionals integrating them into daily clinical practice.

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