



Utilizing Artificial Intelligence in Digital Pathology for Urological Applications: A Comprehensive Review

Kinju Adhikari¹, Talyshinskii Ali, Lingesh Chelliah², Deepak Krishnappa³, Ravi Taori³, Ankit Joshi³, AAdhar Jain⁴, Karthika Rani⁴, Raghunath, S. K.⁴

1. Uro Oncology and Robotic Surgery, HCG Cancer Hospital Bengaluru
2. HCG Cancer Hospital Bengaluru
3. Department of urooncology and robotic surgery, HCG Cancer Hospital Bengaluru
4. Department of urooncology and robotic surgery

Abstract: Purpose: To conduct a scoping review of the literature identifying clinical scenarios for the use of digital pathology (DP) in urology, its advantages, and obstacles to clinical adoption. Material and Methods: A comprehensive literature search was conducted using PubMed/MEDLINE and Google Scholar databases. Search terms included “digital pathology,” “artificial intelligence,” “urology,” “whole slide imaging,” “telepathology,” and “pathology diagnostics.” The PubMed/MEDLINE search yielded 173 articles; supplementary Google Scholar searches and reference-list screening broadened the scope. Inclusion criteria required peer-reviewed studies or reviews addressing AI or DP in a urological context. Studies lacking clinical relevance to genitourinary pathology were excluded. The search strategy and selection process are summarized in Figure 1. Results: In urological pathology, DP enables three-dimensional (3D) pathomorphological reconstruction, improves the accuracy of grading and staging, facilitates intraoperative real-time slice assessment, supports specialist training, and allows large-scale information storage—opening new horizons in telepathology. Artificial intelligence algorithms, difficult to apply in classical light microscopy, offer further significant prospects for pathologists. Despite these advantages, limitations including high equipment costs, large image file sizes, server dependency, data privacy concerns, and the need for specialist training continue to slow widespread adoption. Conclusion: DP empowers urologists, pathologists, and healthcare professionals with tools to achieve more precise diagnoses, personalize treatments, and deliver a new standard of patient care. While challenges accompany this digital transformation, the potential benefits are profound and far-reaching. Future efforts should prioritize standardization, regulatory approval, ethical frameworks, and training to accelerate clinical adoption.

Keywords: Digital Pathology, Artificial Intelligence, Urology, Whole Slide Imaging (WSI), Prostate Cancer, Telepathology, Genitourinary Oncology

INTRODUCTION

For many years, urologists have relied on histopathological examination—a process in which pathologists carefully examine tissue slides under a light microscope. However, inter-observer variability may result from variations in laboratory procedures and subjective interpretation, despite its significance and benefits including low cost and broad availability (1). This may lead to inconsistent diagnoses and influence treatment choices. Since tissue samples are frequently transported from various locations to central laboratories, the process involves logistical challenges and potential delays. Furthermore, microscopic examination is time-intensive, and the constant demand for accurate, timely diagnosis creates significant pressure on pathology services (2).

The practice of urology stands at a crossroads where traditional methodologies intersect with cutting-edge digital technologies. Digital Pathology (DP) emerges as a transformative force poised to redefine how urologists diagnose, treat, and understand urological conditions (3). A digital workflow offers multiple benefits: simplified case sharing and consultation across interdisciplinary teams, standardized education, organized digital slide archiving, and highly reproducible complex data extraction (4). DP leverages high-resolution imaging, computational analysis, and telepathology to create a digital ecosystem where glass slides become globally accessible digital images (5). This review examines the dynamic landscape of DP in urology, its profound implications, manifold advantages, and persistent challenges.

METHODOLOGY

A comprehensive literature search was conducted using PubMed/MEDLINE and Google Scholar databases to explore the utilization of artificial intelligence (AI) in digital pathology for urological applications. Search terms included “digital pathology,” “artificial intelligence,” “urology,” “whole slide imaging,” “telepathology,” and “pathology diagnostics.” The initial PubMed/MEDLINE search yielded 173 articles. Supplementary Google Scholar searches were performed to broaden scope and incorporate diverse perspectives. Reference lists from selected articles were also reviewed to identify additional relevant studies.

Inclusion criteria required peer-reviewed original research or review articles written in English that addressed AI or digital pathology in a urological or genitourinary pathology context. Studies focused exclusively on imaging modalities such as MRI or CT, without pathology components, were excluded, as were conference abstracts and non-peer-reviewed sources. Two independent reviewers screened titles and abstracts, with discrepancies resolved by consensus.

This review adopts a narrative scoping approach, offering flexibility to explore various aspects of AI in digital pathology across multiple urological malignancies. The literature search and selection process are summarized in Figure 1.

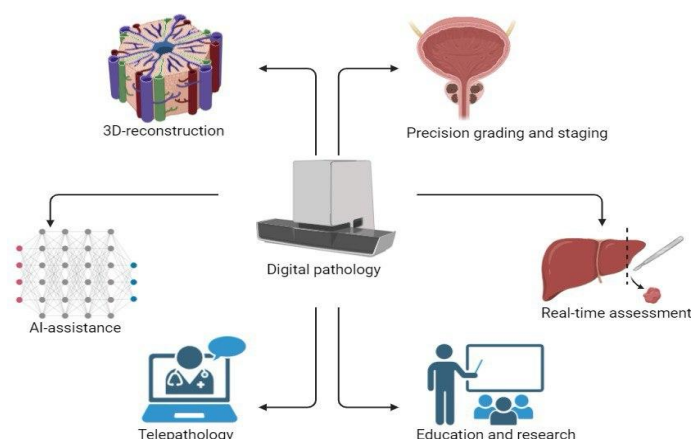


Figure 1: Overview of digital pathology (DP) applications in urology. The central DP scanner enables 3D reconstruction, precision grading and staging, real-time intraoperative assessment, telepathology, education and research, and AI-assisted diagnostics.

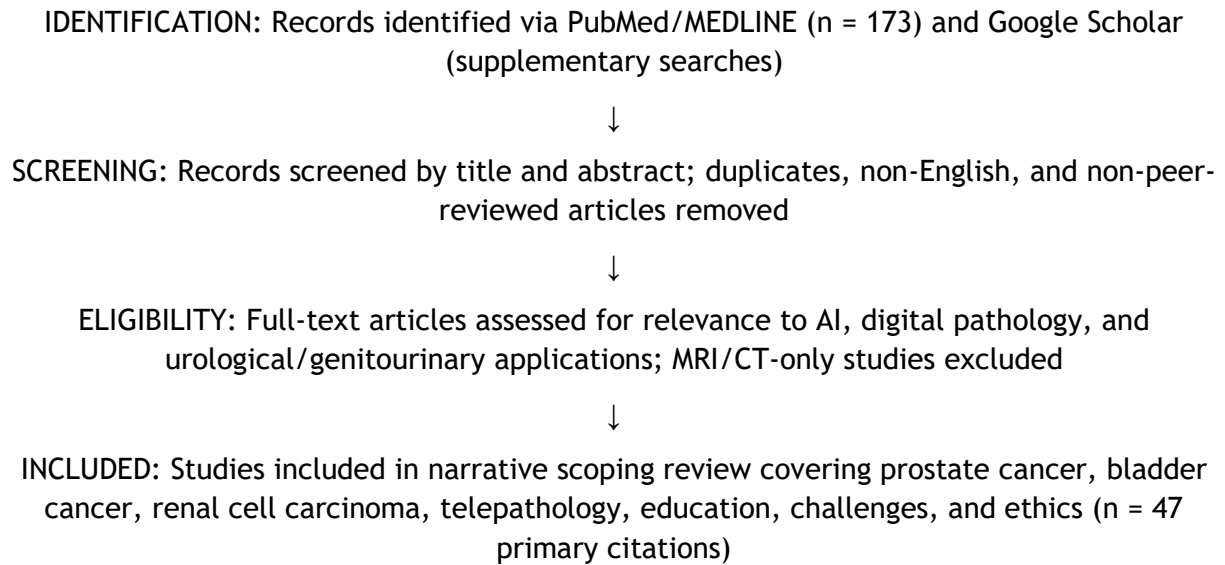


Figure 2: PRISMA-Inspired Literature Search and Selection Flow

WHOLE SLIDE IMAGING (WSI): A GAME CHANGER

The foundation of DP, Whole Slide Imaging (WSI), best exemplifies its revolutionary potential. WSI rapidly digitizes entire glass slides, transcending the limitations of traditional microscopy. Using this method, tissue samples are scanned in their entirety and converted to digital format. The specimen is first scanned globally at low resolution; the resulting image is segmented into “patches” and scanned at maximum resolution, with outputs stored in a pyramidal structure. Using 2,045 cases including genitourinary specimens, Borowsky et al. (6) compared primary diagnoses made by pathologists using WSI versus standard microscopy. The overall major discrepancy rates were 3.64% for WSI review and 3.20% for manual review, a difference of only 0.44%. Average case review time was 5.20 minutes for WSI and 4.95 minutes for glass slides, demonstrating comparable diagnostic performance with significant workflow flexibility.

Table 1: Summary of Key Advantages of Digital Pathology in Urological Practice

Application Area	Clinical Benefit
3D Reconstruction	Enables three-dimensional pathomorphological reconstruction of specimens, reducing sampling and geometric bias.
Enhanced Grading	Increases concordance in Gleason grading; WSI improves kappa from 0.23 to 0.42 vs conventional exam.
Real-Time Margin Assessment	Facilitates intraoperative margin evaluation via fluorescence confocal microscopy, potentially avoiding secondary surgery.
Telepathology	Enables remote expert consultation; reduces transport risk, turnaround time, and geographic barriers to diagnosis.
Education & Training	Supports standardized web-based training; online Gleason grading courses improved interobserver kappa from 0.25 to 0.52.
Digital Archiving	Whole slide imaging allows mass digital storage, eliminates slide breakage risk, and enables simultaneous multi-user access.
AI Integration	AI algorithms automate detection, grading, and survival prediction with AUC values consistently above 0.90 across cancer types.

3D Pathomorphological Reconstruction

Tissue deformation resulting from specimen fixation, cutting, and mounting represents a significant challenge in 3D image reconstruction of histology slides. Standard light microscopy further compromises architectural integrity by sectioning whole slides into quadrants or sextants to fit glass dimensions, introducing sampling and geometric biases. Sampling bias arises from staining, sectioning, and imaging limitations; geometric bias occurs when planar sampling misses structures of interest. Automated WSI substantially reduces these biases by increasing the number of slides and sampled areas. Modern scanners capable of traversing objects in depth (z-stacks) can generate three-dimensional digital representations far more useful for clinical diagnosis. Jansen et al. (7) demonstrated 3D reconstruction and visualization from sequential 2D bladder cancer en-bloc specimens across 21 patients, achieving accurate registration in 13 of 16 evaluable cases and enabling full 3D visualization of tumor-muscularis propria spatial relationships.

Precision in Grading and Staging

Accurate grading and staging are paramount in urological oncology, yet histopathology remains known for interobserver variability. Interobserver studies in prostate cancer show only moderate agreement when assessing Gleason score (8). Evans et al. (9) found good-to-excellent agreement among expert urological pathologists assessing extra-prostatic extension and surgical margin status on WSI. Prostatic adenocarcinoma Gleason grading is particularly well-suited to DP, as the suspicious area is frequently small, enabling fast scanning with smaller file sizes. Chargari et al. (10) assessed 816 prostate needle biopsy cores in 68 consecutive patients: concordance with definitive radical prostatectomy scores improved dramatically from 54.4% ($\kappa = 0.23$) with conventional examination to 66.2% ($\kappa = 0.42$) with WSI—representing a clinically meaningful improvement.

Real-Time Intraoperative Assessment

In uro-oncology, real-time margin assessment can determine whether a patient requires a single procedure or multiple interventions. DP facilitates prompt margin assessment with high-resolution digital images, potentially avoiding secondary surgeries. This is particularly critical in procedures such as NeuroSAFE during radical prostatectomy, where margin assessment determines the need for secondary resection (11). Rocco et al. (12) evaluated digital biopsies using fluorescence confocal microscopy (FCM), achieving 95.1% correct diagnosis with near-perfect inter-rater agreement for PCa detection ($\kappa = 0.84$ for FCM). A subsequent study by Rocco et al. (13) presented an alternate NeuroSAFE approach using digital frozen sections and FCM during robot-assisted radical prostatectomy; all patients demonstrated negative surgical margins at final histology, with four undergoing subsequent resection to achieve negative status.

Education and Research

WSI technology eliminates the need for multiple physical slide copies or microscopes, enables slide annotation, and supports standardized international education. The American Board of Pathology and several examining boards have transitioned to fully virtual slide

formats (14). Web-based Gleason grading courses using WSI have demonstrated improved interobserver agreement: Abdollahi et al. (16) reported improvement in mean interobserver kappa from 0.25 before to 0.52 after web-based instruction. The International Society of Urological Pathology (ISUP) online prostate pathology course enrolled 603 pathologists across nine countries; the proportion of correct diagnoses rose from 60.7% to 72.3% between pre- and post-lecture evaluations, with notable improvement in low-resource settings (47.4% to 62.8%) (17). Additionally, Fedorov et al. (18) demonstrated superior WSI-MRI correlation compared to standard surgical pathology reports for index lesion localization.

Telepathology

WSI/virtual microscopy technology enables simultaneous slide viewing from multiple locations, providing expert second opinions and side-by-side comparative viewing. Since its inception in the 1980s, dynamic-robotic telepathology has proven particularly significant for urologists managing distant uropathology cases in real-time (19). Telepathology offers lower long-term costs, reduced risk of slide loss or breakage, elimination of unnecessary paperwork, faster turnaround times, and efficient workload distribution. The technology addresses geographic disparities: for example, the shortage of pathologists in sub-Saharan Africa significantly delays prostate cancer detection (20). Girolami et al. (21) reported 2,058 intraoperative telepathology consultations in South Tyrol, achieving 100% specificity with no false-positive cases, demonstrating clinical reliability for frozen section diagnosis.

THE ROLE OF ARTIFICIAL INTELLIGENCE (AI)

AI-based computational pathology was pioneered by Fuchs et al. (22), who developed an automated image analysis pipeline using tissue microarray analysis to forecast renal clear cell carcinoma prognosis, with a random forest classifier performing comparably to skilled pathologists. Advances in technology and precision medicine have since enabled AI-based solutions for quantitative pathologic assessment, extracting information beyond the scope of human visual perception and substantially automating time-consuming tasks.

Renal Cell Carcinoma

Gondim et al. (23) constructed an AI model correctly classifying 47 of 55 (85%) WSIs across five RCC subtypes. Abdeltawab et al. (24) proposed a pyramidal deep learning pipeline achieving AUC of 0.92 for distinguishing clear cell RCC from clear cell papillary RCC. Wessels et al. (25) developed DINO-ViT, a self-supervised vision transformer predicting overall and disease-specific survival in ccRCC; it was a significant predictor of overall survival in training (HR 3.03; $p < 0.01$) and disease-specific survival in validation (HR 2.31; $p = 0.02$).

Prostate Cancer

Zhdanovich et al. (26) evaluated machine learning models classifying prostate cancer versus hyperplastic tissue using TMA cores, achieving best AUC of 0.93 for PIN-4 staining. Singhal et al. (27) reported AUC values of 0.990, 0.960, and 0.930 for low- versus high-grade tumor

detection across three test sets, and 0.900, 0.920, and 0.830 for differentiating Gleason grade groups 2 and 3—performance rivaling expert pathologists.

Bladder Cancer

Niazi et al. (28) developed a multi-class segmentation model for bladder biopsy layers, achieving an average expert-assessed accuracy of 8.93/10. Yin et al. (29) distinguished non-invasive (Ta) from superficially invasive (T1) bladder cancer with 91-96% accuracy using machine learning and 84% with CNN-based methods. Wu et al. (30) created a lymph node metastases diagnostic model enabling pathologists to reject 80-92% of negative slides while maintaining 100% sensitivity. Tsuneki et al. (31) applied deep learning for urothelial carcinoma screening on liquid-based cytology WSIs, achieving AUC of 0.984-0.990. Wu et al. (32) combined radiological and pathological features for molecular subtype prediction in bladder cancer, achieving AUC of 0.89 with the multimodal approach. Mi et al. (33) developed an ML model predicting response to neoadjuvant chemotherapy in muscle-invasive bladder cancer with 65-73% accuracy.

CHALLENGES ON THE DIGITAL PATH

Infrastructure and Cost

Despite DP's advantages over traditional microscopy, several barriers slow widespread adoption. High-quality slide scanners and high-resolution color monitors remain expensive, though costs are expected to decrease over time. Monitor calibration for brightness, contrast, and resolution is essential, and many displays continue to exhibit off-angle color shifts. Image loading speed depends on internet connectivity and server proximity. A single uncompressed prostate biopsy WSI may occupy 1-5 GB of storage; a full prostate biopsy set comprising multiple cores at different levels generates a substantial data burden per case (34).

Standardization and Validation

The broad variety of WSI scanners produces significant variances in image quality. Standardization and regulatory validation—including FDA clearance—are vital to ensure consistent digitization outcomes (35-38). Duenweg et al. (38) found significant differences in mean color channel intensity between scanner models (all $p < 0.001$). While intra-laboratory variation may be manageable with quality assurance schemes such as ISO 15189 (41), inter-institutional cohort variability is more problematic—particularly relevant when using datasets such as TCGA, which accounted for approximately 42% of AI-based bladder cancer pathology studies in one recent systematic review (42). Most modern scanners incorporate quality control systems (43), and AI-based control modalities are emerging (44).

Ethical and Legal Considerations

Ethical considerations surround patient data privacy and consent, particularly when AI algorithms are trained on large datasets containing sensitive health information. Ensuring patient confidentiality, informed consent, and transparent communication about AI's

diagnostic role is essential. Algorithmic bias—which may disproportionately impact certain patient populations—underscores the need for rigorous validation and ongoing monitoring (36, 37). Legal challenges include liability for diagnostic errors, intellectual property rights over AI algorithms, and regulatory compliance with healthcare standards. Clear guidelines and regulatory frameworks are required to ensure responsible AI deployment in urological pathology while maintaining patient safety and ethical standards.

Workflow Integration and Training

Navigating virtual slides with a computer mouse differs substantially from using a microscope stage. Van der Kwast et al. (44) investigated interobserver variability in WSI assessment of atypical foci in prostate biopsies among 12 pathologists and found poor consensus even among experts, partly attributed to unfamiliarity with WSI viewing. Incorporating WSI into routine surgical pathology practice requires modifications to workflow patterns and ergonomics, including addressing repetitive computer injuries such as carpal tunnel syndrome (45).

CONCLUSION

Digital Pathology represents a fundamental transformation in urological diagnostics. This review demonstrates that AI-integrated DP meaningfully improves the accuracy of Gleason grading, facilitates real-time margin assessment, enables 3D tumor reconstruction, enhances educational outcomes, and extends diagnostic access globally through telepathology.

To accelerate clinical translation, three priority areas require coordinated action: (1) Standardization—international consensus on scanner validation protocols and image quality benchmarks, aligned with regulatory frameworks (FDA, CE marking) to ensure cross-institutional comparability; (2) Ethical and legal infrastructure—transparent AI governance frameworks addressing data privacy, informed consent, liability, and algorithmic bias, particularly for vulnerable or under-represented populations; and (3) Workforce development—structured training programs integrating WSI and AI literacy into pathology and urology curricula at all career stages. The evidence reviewed here positions DP not as a future aspiration but as a present capability awaiting systematic implementation. Collaborative investment by clinicians, health systems, regulators, and technology developers is now the critical step toward realizing its full diagnostic and therapeutic potential.

REFERENCES

1. Barisoni L, et al. Digital pathology evaluation in the multicenter Nephrotic Syndrome Study Network (NEPTUNE). *Clin J Am Soc Nephrol*. 2013;8(8):1449-59.
2. Williams BJ, Bottoms D, Treanor D. Future-proofing pathology: the case for clinical adoption of digital pathology. *J Clin Pathol*. 2017;70(12):1010-8.
3. Weinstein RS, et al. Telepathology overview: from concept to implementation. *Hum Pathol*. 2001;32(12):1283-99.

4. Aeffner F, et al. Roles for Pathologists in a High-throughput Image Analysis Team. *Toxicol Pathol.* 2016;44(6):825-34.
5. Blom S, et al. Systems pathology by multiplexed immunohistochemistry and whole-slide digital image analysis. *Sci Rep.* 2017;7(1):1-13.
6. Borowsky AD, et al. Digital Whole Slide Imaging Compared With Light Microscopy for Primary Diagnosis in Surgical Pathology. *Arch Pathol Lab Med.* 2020;144(10):1245-53.
7. Jansen I, et al. Three-dimensional histopathological reconstruction of bladder tumours. *Diagn Pathol.* 2019;14(1).
8. Ozkan TA, et al. Interobserver variability in Gleason histological grading of prostate cancer. *Scand J Urol.* 2016;50(6):420-4.
9. Evans AJ, et al. Interobserver variability between expert urologic pathologists for extraprostatic extension and surgical margin status in radical prostatectomy specimens. *Am J Surg Pathol.* 2008;32(10):1503-12.
10. Chargari C, et al. Prostate needle biopsy examination by means of virtual microscopy. *Pathol Res Pract.* 2011;207(6):366-9.
11. Taori R, et al. Neurovascular Structure-Adjacent Frozen-Section Examination (NeuroSAFE) Technique of Nerve-Sparing RARP: Technique, Feasibility, and Early Outcomes. *Indian J Surg Oncol.* 2024 Feb.
12. Rocco B, et al. Digital Biopsy with Fluorescence Confocal Microscope for Effective Real-time Diagnosis of Prostate Cancer. *Eur Urol Oncol.* 2021;4(5):784-91.
13. Rocco B, et al. Digital Frozen Sections with Fluorescence Confocal Microscopy During Robot-assisted Radical Prostatectomy: Surgical Technique. *Eur Urol.* 2021;80(6):724-9.
14. Hassell LA, et al. Pathology Education Powered by Virtual and Digital Transformation: Now and the Future. *Arch Pathol Lab Med.* 2023;147(4):474-91.
15. Helin H, et al. Web-based virtual microscopy in teaching and standardizing Gleason grading. *Hum Pathol.* 2005;36(4):381-6.
16. Abdollahi A, et al. Inter/Intra-observer reproducibility of Gleason scoring in prostate adenocarcinoma in Iranian pathologists. *Urol J.* 2012;9(2):486-90.
17. Egevad L, et al. The International Society of Urological Pathology Education web—a web-based system for training and testing of pathologists. *Virchows Arch.* 2019;474(5):577-84.
18. Fedorov A, et al. The role of pathology correlation approach in prostate cancer index lesion detection with multiparametric MRI. *Acad Radiol.* 2015;22(5):548-55.
19. Weinstein R, Holcomb M, Krupinski E. Invention and Early History of Telepathology (1985-2000). *J Pathol Inform.* 2019;10(1):1.
20. Farré X, Kibera J. The untapped potential of digital pathology in prostate cancer diagnosis and medical education in sub-Saharan Africa. *African J Urol.* 2018;24(1):54-5.
21. Girolami I, et al. Frozen section telepathology service: Efficiency and benefits of an e-health policy in South Tyrol. *Digit Health.* 2022;8.
22. Fuchs TJ, et al. Computational pathology analysis of tissue microarrays predicts survival of renal clear cell carcinoma patients. *Med Image Comput Comput Assist Interv.* 2008;11(Pt 2):1-8.
23. Gondim DD, et al. Artificial intelligence-based multi-class histopathologic classification of kidney neoplasms. *J Pathol Inform.* 2023;14.

24. Abdeltawab H, et al. A pyramidal deep learning pipeline for kidney whole-slide histology images classification. *Sci Rep.* 2021;11(1).
25. Wessels F, et al. A self-supervised vision transformer to predict survival from histopathology in renal cell carcinoma. *World J Urol.* 2023;41(8):2233-41.
26. Zhdanovich Y, et al. Evaluation of automatic discrimination between benign and malignant prostate tissue in the era of high precision digital pathology. *BMC Bioinformatics.* 2023;24(1).
27. Singhal N, et al. A deep learning system for prostate cancer diagnosis and grading in whole slide images of core needle biopsies. *Sci Rep.* 2022;12(1):1-11.
28. Niazi MKK, et al. Semantic segmentation to identify bladder layers from H&E Images. *Diagn Pathol.* 2020;15(1).
29. Yin PN, et al. Histopathological distinction of non-invasive and invasive bladder cancers using machine learning approaches. *BMC Med Inform Decis Mak.* 2020;20(1).
30. Wu S, et al. Artificial intelligence-based model for lymph node metastases detection on whole slide images in bladder cancer. *Lancet Oncol.* 2023;24(4):360-70.
31. Tsuneki M, et al. Deep Learning-Based Screening of Urothelial Carcinoma in Whole Slide Images of Liquid-Based Cytology Urine Specimens. *Cancers (Basel).* 2022;15(1).
32. Wu P, et al. Multimodal investigation of bladder cancer data based on computed tomography, whole slide imaging, and transcriptomics. *Quant Imaging Med Surg.* 2023;13(2):1023-35.
33. Mi H, et al. Predictive models of response to neoadjuvant chemotherapy in muscle-invasive bladder cancer using nuclear morphology and tissue architecture. *Cell Rep Med.* 2021;2(9):100382.
34. Jansen I, et al. Histopathology: ditch the slides, because digital and 3D are on show. *World J Urol.* 2018;36(4):549-55.
35. Babawale M, et al. Verification and Validation of Digital Pathology (Whole Slide Imaging) for Primary Histopathological Diagnosis: All Wales Experience. *J Pathol Inform.* 2021;12(1).
36. Adhikari K, et al. Exploring the ethical, legal, and social implications of ChatGPT in urology. *Curr Urol Rep.* 2024;25(1):1-8.
37. Naik N, et al. Legal and ethical consideration in artificial intelligence in healthcare: who takes responsibility? *Front Surg.* 2022;9:266.
38. Duenweg SR, et al. Whole slide imaging (WSI) scanner differences influence optical and computed properties of digitized prostate cancer histology. *J Pathol Inform.* 2023;14.
39. Baxi V, et al. Digital pathology and artificial intelligence in translational medicine and clinical practice. *Mod Pathol.* 2022;35(1):23-32.
40. Tzankov A, Tornillo L. Hands-On Experience: Accreditation of Pathology Laboratories according to ISO 15189. *Pathobiology.* 2017;84(3):121-9.
41. Khoraminia F, et al. Artificial Intelligence in Digital Pathology for Bladder Cancer: Hype or Hope? A Systematic Review. *Cancers (Basel).* 2023;15(18).
42. Aeffner F, et al. Introduction to Digital Image Analysis in Whole-slide Imaging: A White Paper from the Digital Pathology Association. *J Pathol Inform.* 2019;10(1).
43. Haghighat M, et al. Automated quality assessment of large digitised histology cohorts by artificial intelligence. *Sci Rep.* 2022;12(1).
44. Van Der Kwast TH, et al. Variability in diagnostic opinion among pathologists for single small atypical foci in prostate biopsies. *Am J Surg Pathol.* 2010;34(2):169-77.

45. Shiri R, Falah-Hassani K. Computer use and carpal tunnel syndrome: A meta-analysis. *J Neurol Sci.* 2015;349(1-2):15-9.
46. Roessler N, et al. Digital pathology-based artificial intelligence for individualized urologic cancer care: a systematic review. *Eur Urol Focus.* 2025;S2405-4569(25)00362-1. doi:10.1016/j.euf.2025.12.007.
47. Ni HM, Kouzy R, Sabbagh A, et al. The state of the art in artificial intelligence and digital pathology in prostate cancer. *Nat Rev Urol.* 2026;23:13-28.