

# Artificial Intelligence in Diagnostic Pathology: A Narrative review on Current Applications, Emerging Challenges, and Future Perspectives

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## ABSTRACT

Advancements in digital pathology and whole-slide imaging have enabled Artificial Intelligence (AI) to emerge as a transformative tool in diagnostic pathology. AI has enabled the automated analysis of histopathological images, improving diagnostic accuracy and reproducibility, as well as workflow efficiency. The aim of this narrative review is to provide a comprehensive overview of current applications of AI in diagnostic pathology, including tumour detection, grading, biomarker prediction, and subspecialty-specific applications, clinical utility, technical advances, along with challenges and future perspectives. The prediction of molecular alterations and therapeutic response directly from histopathological images is also made possible by AI. Cross-domain prediction and precision oncology have been further advanced by evolving technologies such as multimodal AI and foundation models. However, existing challenges such as data heterogeneity, annotation bias, lack of standardisation, limited interpretability, and regulatory constraints restrict its widespread clinical implementation. Although AI has shown significant promise in improving diagnostic accuracy, its optimal utilisation lies in a collaborative framework in which AI serves as a decision-support tool rather than a replacement for pathologists. Emerging approaches such as Explainable AI (XAI), foundation models, and multimodal AI integrating histopathology with genomic and clinical data are expected to enhance clinical translation and precision oncology. Future research focusing on large, multi-institutional datasets, prospective validation, and integration of multimodal data is needed to enable reliable clinical acceptance.

**Keywords:** Computational pathology, Deep learning, Digital pathology, Histopathology, Precision medicine, Whole-slide imaging

## INTRODUCTION

Cancer is a major global health burden. According to the GLOBOCAN 2022 estimates, approximately 19.96 million new cancer cases and 9.7 million cancer-related deaths occurred worldwide in 2022. With population aging and lifestyle changes, the incidence is still increasing, making early diagnosis and effective management critical challenges [1]. Accurate diagnosis is a key element of cancer management, with histopathological evaluation serving as the basis of clinical decision-making.

Diagnostic pathology depends upon microscopy of Haematoxylin and Eosin (H&E) stained tissue sections. Along with Immunohistochemistry (IHC) and molecular testing, these methods classify disease and predict outcomes. However, traditional approaches are inherently subjective, and affected by interobserver variability, workload, and case complexity [2].

AI is reshaping medicine by building on these advancements. Being a computer science stream, AI helps machines to learn from data and perform tasks in which human insight is needed. The utility of AI is rising in histopathology because of large image datasets, refined algorithms, and significantly increased processing power. Deep Learning (DL) and Machine Learning (ML) can detect patterns that the human eye fails to capture, aiding the analysis of complex images [3].

Because of these advancements, AI integration has enabled the switch from traditional microscopic evaluation to digital pathology, where glass slides are converted into high-resolution Whole-Slide Images (WSIs). Thus, remote consultation, image sharing, and large-scale data storage are facilitated by these WSIs. These systems form the technological foundation for the integration of

AI in pathology workflows. The availability of large-scale digital datasets has enabled the application of ML and DL techniques in computational pathology. These AI-based approaches have shown utility in tasks like tumour detection, classification, prediction of molecular alterations, therapeutic response, prognosis, and biomarker discovery. More importantly, AI detects unknown morphological patterns and helps in automated diagnostics thereby creating novel image-based biomarkers from the histopathology data. There is increasing interest in integrating AI with multi-omics and clinical data to improve personalised cancer care [4].

Despite these advancements, several challenges limit clinical implementation. The key barriers are data heterogeneity, lack of standardised infrastructure, and limited algorithm interpretability. Regulatory as well as ethical issues like privacy and bias also slow down the progress. The high cost of digital pathology, together with the need for validation studies, further limits the widespread approval.

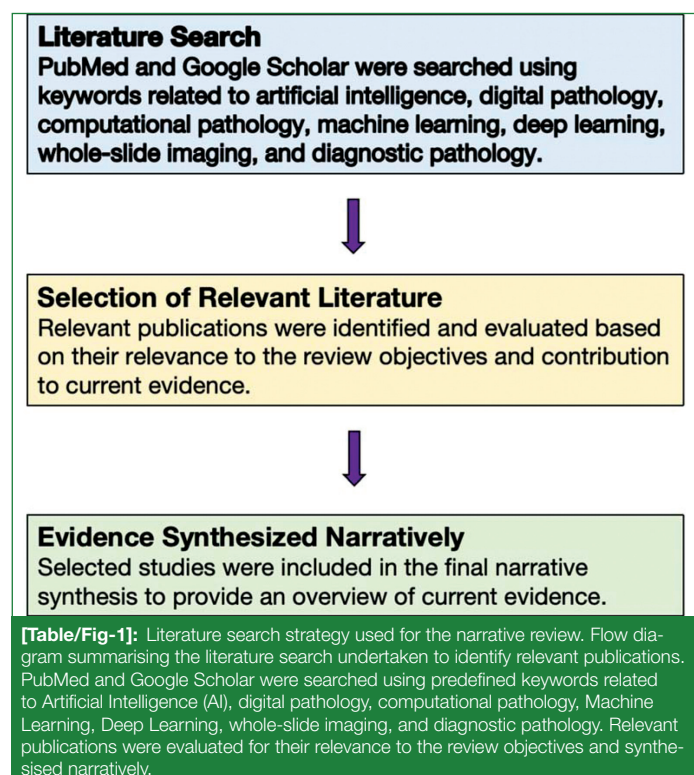
This narrative review aims to provide a comprehensive overview of AI in diagnostic pathology, focusing on technological developments, clinical applications, validation challenges, and emerging directions including XAI, foundation models, and multimodal integration.

## Literature Search Strategy

A narrative review of the literature was conducted to summarise the current applications, challenges, and future directions of AI in diagnostic pathology. Relevant articles were identified through electronic searches of PubMed and Google Scholar. The literature search primarily focused on studies published between January 2020 and March 2026, with selected earlier landmark studies included for foundational context.

The search included combinations of the keywords like “AI”, “digital pathology”, “computational pathology”, “histopathology”, “ML”, “DL”, “whole-slide imaging”, and “diagnostic pathology” using Boolean operators (AND/OR). Relevant original research articles, systematic reviews, meta-analyses, and review articles addressing various applications of AI in diagnostic pathology publications were selected according to their relevance, scientific quality, and contribution to achieving the objectives of this review, with an emphasis on clinically applicable and contemporary findings. The selected literature was qualitatively analysed to provide a comprehensive overview of current advancements, clinical applications, limitations, and future directions of AI in diagnostic pathology.

[Table/Fig-1] illustrates the literature search process and study selection procedure utilised for this review, which includes search in databases, screening, eligibility evaluation, and the final incorporation of studies.



## Framework of Artificial Intelligence (AI) in Diagnostic Pathology

This section explains the conceptual and practical framework of AI in diagnostic pathology, spanning technology development, validation, clinical applications, and future directions.

### Digital Pathology: Foundation for AI

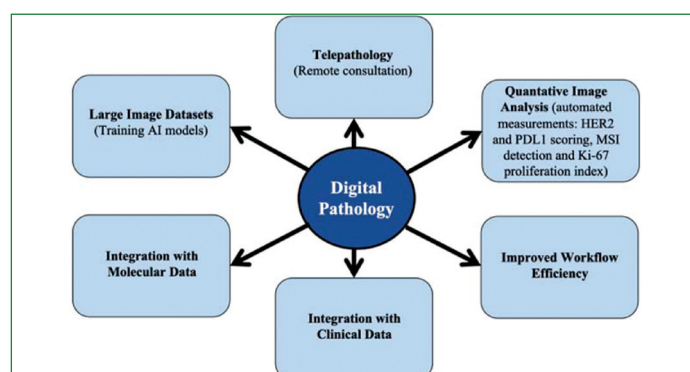
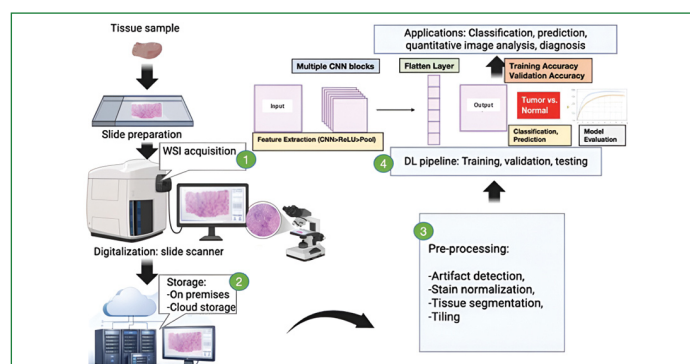
Digital pathology means converting conventional tissue analysis into a digital process and providing the technology needed to develop and apply AI in diagnostic pathology. In the past, tissue sample examination meant looking at glass slides under a microscope, which was dependent on the expertise of pathologists and could lead to pinions. Now, with digital pathology, pathologists can view tissue samples on screens and analyse them with computer algorithms after converting glass slides into sharp digital images [5].

The WSI is the foundation of digital pathology where scanner scans entire histopathology slides and generates elaborated digital images. The information seen under traditional microscopes can match closely to that in high-resolution images, which can reach up to very high magnifications. After the scanning process, images are integrated with clinical data and processed for storage, sharing, and analysis with the help of specialised software. This infrastructure enables remote consultation, telepathology, education, and AI-based image analysis [5].

Digital pathology workflow includes slide digitalisation, preprocessing, and computational analysis. All these steps are very important so as to remove the background noise and maintain the quality of the image across all datasets. Once the images are ready, DL and ML can extract useful features from tissue structures [5]. Large-scale data storage and collaborative research is facilitated by the digital slide archives which enables the development of large annotated datasets that are needed to train these AI models. In pathology labs, these features greatly enhance research collaboration, educational possibilities, and workflow efficiency [6].

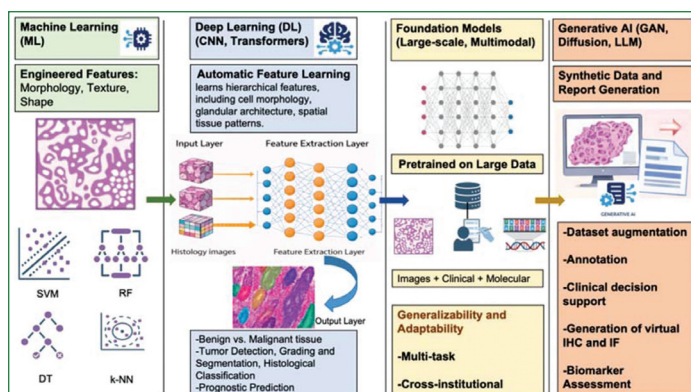
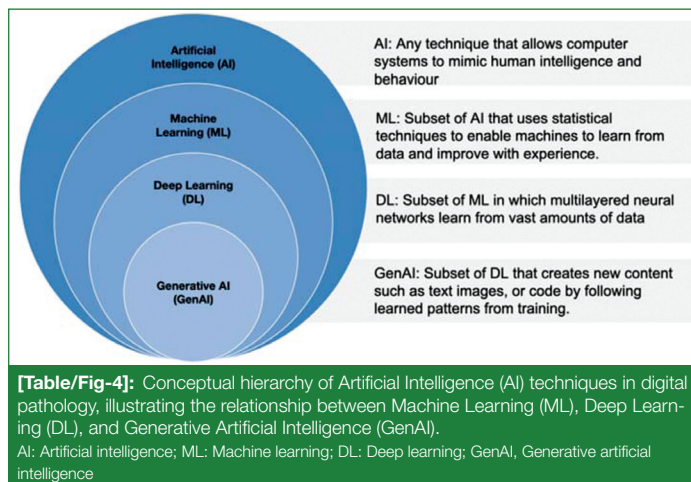
In recent times, digital image analysis and AI models are being used in daily pathology practices. The effective implementation of AI-driven diagnostic techniques in clinical setups depends on the deployment of infrastructure for digital pathology, as has been shown by global initiatives such as the Swiss Digital Pathology Consortium. This includes authorised scanners, tools for image management, and standardised workflows [7].

Thus, digital pathology is the key technical platform that has made it possible to use AI in diagnostic pathology. Large-scale data storage capacity, sophisticated computational algorithms, and high-resolution digital imaging have revolutionised the pathology discipline. This revolution is showing the path to more accurate, efficacious, and data-based approaches towards diagnosis. AI-enabled workflow in digital pathology has been illustrated in [Table/Fig-2]. The advantages of digital pathology which provides the technological foundation for the development and clinical implementation of AI in diagnostic pathology has been illustrated in [Table/Fig-3]. Once the digital pathology infrastructure has been established, different AI tools can be utilised to evaluate WSI and develop clinically useful insights.



## AI Development and Technologies

The AI models assess digital WSIs to identify patterns that are related to diagnosis, in digital pathology. These models include conventional ML algorithms, advanced DL and foundation models, and emerging generative AI approaches [8]. [Table/Fig-4] illustrates the definitions and hierarchy of methodologies used in AI. [Table/Fig-5] illustrates how the evolution of AI technologies has transformed digital pathology in terms of diagnosis, prognosis, and precision medicine.



Conventional ML approaches depend on engineered features such as morphology, texture, and shape to perform classification tasks in histopathological images. Classifiers like Support Vector Machine (SVM), Random Forest (RF), Decision Tree (DT), and k-Nearest Neighbour (k-NN) are used to examine these features so as to perform tasks like normal tissue versus tumour classification, characterisation of lesions as benign or malignant, and prediction of histological subtype [9]. In contrast, DL models, especially CNNs and transformer-based models, learn complex hierarchical characteristics from WSIs, which enables applications such as tumour detection, histological classification, tumour grading, and segmentation [10]. Weakly supervised learning approaches, especially multi-instance learning, make it possible to train using slide-level annotations without requiring detailed pixel-level labelling. This helps in decreasing annotation burden in WSI analysis. Recently, foundation models trained on large multimodal datasets, integrating histopathology images with clinical, and molecular data, have enabled cross-organ analysis and multi-task prediction. In digital pathology workflows, the generation of synthetic images, automated report production, dataset augmentation, and clinical decision support are further supported by emerging generative

AI techniques, such as Generative Adversarial Networks (GAN), diffusion models, and Large Language Models (LLM). Virtual IHC or Immunofluorescence (IF) images can be created straightaway from digital (H&E) slides with the assistance of DL models including GANs and diffusion models [11,12]. These techniques may quicken the assessment of biomarkers and cut down laboratory costs. Right after the generation of AI models, comprehensive validation is necessary to establish their accuracy in diagnosis, ability to reproduce, and clinical significance [9].

## Validation and Diagnostic Performance

The diagnostic efficacy of AI algorithms in digital pathology has been assessed in a number of systematic studies and meta-analyses. These studies repeatedly indicate that AI systems may achieve diagnostic accuracy similar to expert pathologists in certain tasks such as tumour detection, classification, grading, and biomarker prediction from histopathological images. Due to the integration of AI with WSI, large histopathology datasets may now be analysed automatically, enabling algorithms to detect subtle morphologic characteristics that human observers might find hard to detect [10,13].

AI models in neuropathology have demonstrated encouraging outcomes in the identification and categorisation of paediatric brain tumours. A mean diagnosis accuracy of almost 91.3%, with sensitivity reaching 94.2% and specificity 97.4%, was found in a comprehensive study assessing AI-based models for the detection and subtyping of medulloblastoma from histopathology pictures. The ability of AI to detect tumour existence and architectural patterns on histology slides is demonstrated by the fact that detection tasks typically outperformed molecular or subtype classification tasks. These results imply that AI could be a useful supplementary tool for enhancing diagnosis accuracy in the pathology of paediatric brain tumours [13].

In a similar manner, in gastrointestinal oncology, AI has proven to be highly effective in the detection of HCC. Depending upon the validation dataset, a recent meta-analysis assessing AI systems for HCC detection found pooled sensitivity of roughly 84-85% with specificity that range from 84% to 92%. These findings show that in some image-analysis tasks, including screening alongside lesion detection processes, AI systems can reach diagnostic performance on par with or better than that of doctors [14].

In genitourinary pathology, AI models have demonstrated excellent diagnostic accuracy in prostate carcinoma detection and Gleason grading on digital biopsy slides. These models help in obtaining Area-Under-the-Curve (AUC) values close to 0.98-0.99 in validation datasets [15]. Such results demonstrate how AI may increase standardisation in histopathologic evaluation and lower diagnostic variability.

In spite of these positive results, most studies emphasise that AI should be used as a supporting tool rather than a pathologists' replacement [2,4]. Biases in dataset quality, variations in slide preparation, or staining may influence the generalisability of AI algorithms [4]. Thus, the idealistic diagnostic model is one that entails a collaborative strategy in which AI technologies serve as a decision support tool, while pathologists retain final diagnostic responsibility [2]. In digital pathology, this type of "human-AI synergy" enhances workflow efficiency, improves diagnostic accuracy, and decreases effort. Following a successful validation, the AI-based tools can be incorporated into day-to-day pathology workflow processes and deployed across numerous pathology subspecialties [2,4].

## Clinical Integration and Applications across Subspecialties

**Tumour Detection and Classification:** One of the most important applications of AI in pathology is the automated detection and tumour categorisation in histopathological and medical imaging

data. Complex histomorphological patterns in large histology image datasets can be recognised with the help of DL models like CNNs, enabling accurate differentiation between tumour and normal tissue and several tumour subtypes [16].

Prognostication in several malignancies is also aided by AI-based image analysis, which automates the detection and quantification of tumour necrosis. AI algorithms support cancer staging and treatment planning by accurately detecting lymph node metastases on histology slides. For detection of perineural and vascular invasion, which are important predictors of tumour aggressiveness and metastatic potential, DL models have been investigated.

### AI for Biomarker Quantification and Molecular Prediction

In cancer pathology, AI is being used more and more to both find new biomarkers and quantify existing ones. IHC, which is used in daily pathology practice to assess various biomarkers, is prone to observer variability and is also time-consuming. AI models can automate biomarker evaluation and also increase reproducibility. For instance, AI systems have proven to be highly accurate in quantifying biomarkers such as HER2, PD-L1, and Ki-67, which helps pathologists make therapeutic decisions and lowers scoring variability [4].

In addition to well-known biomarkers, novel image-derived biomarkers can also be detected in real time from routine H&E slides. Subtle morphology patterns that correspond to underlying molecular changes can be detected by DL models. Research has demonstrated that AI can use histological images to predict genetic traits such as Homologous Recombination Deficiency (HRD) in breast carcinoma, *BRAF* mutations, *EGFR* mutations in lung cancer, and Microsatellite Instability (MSI) in colorectal cancer [4].

The consolidation of molecular and clinical data with histopathology data to produce predictive biomarkers is possible due to the evolution of foundation models and multimodal AI systems. These AI-derived biomarkers act as digital substitutes for molecular testing, making the precision oncology more accessible and cheap. However, before routine clinical implementation, they must undergo rigorous clinical validation.

AI models may provide additional prognostic information by the quantification of the components of the Tumour Microenvironment (TME), which includes tumour-infiltrating lymphocytes, Tumour-Stroma Ratio (TSR), and stromal features. The quantification of the TSR from histopathological images is made possible by AI-based segmentation algorithms. A high TSR, which reflects a stromal-rich TME, correlates with increased tumour invasion, metastasis and poor clinical outcomes in several malignancies. Commonly used AI segmentation models like U-Net, DeepLab, and Transformer-based are opted to segment glands, tissue and cells for TME analysis. Prediction of patient survival, therapeutic response, and recurrence risk is now possible due to extraction of prognostic features right away from the histopathological images by the DL models. By the integration of histological patterns with clinical and genomic data, DL models have shown promise in predicting response to neoadjuvant therapy and benefit from immunotherapy [10].

The application of AI across various subspecialties of pathology has been encouraged because of such advancements.

**Subspecialty Applications:** AI applications in diagnostic pathology span multiple organ systems, with varying levels of clinical maturity across subspecialties.

### Breast Pathology

The AI is being used extensively in breast pathology, helping in diagnosis, grading, and biomarker assessment. DL models trained on sizable annotated datasets enable detection of tumours, along with identification of subtypes like ductal, lobular, etc., with classification

accuracies exceeding 90%, distinction between benign and malignant lesions, tumour localisation, and quantification of tumour extent [16]. AI also aids in the histological grading of breast carcinoma, namely by automating the assessment of the Nottingham grading elements, such as nuclear pleomorphism, tubule development, and mitotic activity. Automated mitotic detection systems are able to detect mitosis and increase reproducibility as compared to human counting.

Additionally, AI systems are helping identification of lymph node metastases, including isolated tumour cells and micrometastases, leading to increased diagnostic sensitivity and reduced interpretation time. AI-based image analysis is frequently employed for quantification of biomarkers such as ER, PR, HER2, and Ki-67 proliferation index, rendering more objective and reproducible grading. In addition to routine diagnostic tasks, AI algorithms have been examined to predict prognosis, therapy response, and molecular alterations straightaway from the histologic images [17].

### Gastrointestinal Pathology

In the discipline of gastrointestinal pathology, DL models, particularly CNNs, have shown considerable potential. By analysing WSIs, these algorithms have the capability of accurate identification and categorisation of colorectal carcinomas as well as precursor lesions. In several studies, CNN models trained on histopathology images, have performed comparably to expert pathologists in differentiating normal tissue from adenomas and carcinomas. Reported sensitivities of approximately 97% and diagnostic accuracies of approximately 96% have been described for the classification of colorectal polyps, together with the ability to distinguish between polyp subtypes. This indicates that AI can help clinicians to find microscopic abnormalities that might otherwise be missed [18]. AI models are capable of extracting prognostic and predictive data from standard H&E slides in addition to diagnosis. Using DL-based studies, the prediction of tumour subtypes associated with patient outcomes and molecular alterations, such as MSI, can also be made possible. AI models have also been investigated for automated detection of dysplasia in Barrett's oesophagus and for quantification of tumour budding in colorectal carcinoma. These findings suggest that in gastrointestinal and colorectal cancers, AI-derived histomorphologic patterns could act as digital biomarkers of tumour prognosis and behaviour [19]. Recently, a meta-analysis has found the potential of AI-driven models applied to radiological imaging reported a pooled sensitivity of approximately 84% and specificity of up to 92% for the diagnosis of HCC at internal validation, with specificity falling to 84% on external validation [14].

Although most of the research is still retrospective, significant multicentre datasets and prospective validation are required before routine clinical implementation [19].

### Genitourinary Pathology

In genitourinary pathology, AI applications span prostate, renal, bladder, and testicular diseases. AI models assist in tumour detection and classification, enabling differentiation between benign and malignant lesions across prostate and bladder biopsies. In prostate carcinoma, the AI-driven systems can automate quantification of tumour burden, and other histopathological parameters and also support Gleason grading which is playing a decisive role in clinical opinion. In bladder cancer, AI-based techniques have been studied to help with risk stratification and clinical management by predicting tumour progression, lymph-node metastasis, and risk of recurrence. In testicular pathology, ML approaches have been explored for the categorisation of germ cell tumours and evaluation of spermatogenesis in infertility assessment [15,20-23].

The use of digital WSIs in the automatic identification and categorisation of renal pathological lesions has shown great promise for AI. In renal pathology, CNNs, in particular, are DL

models capable of identifying glomerular structures, and detect pathological changes such as sclerosis, interstitial fibrosis, and tubular atrophy, along with inflammatory cell infiltrate. This kind of quantitative analysis makes it possible to predict renal function decline [24]. In renal tumour pathology, AI models can classify histological subtypes of Renal Cell Carcinoma (RCC) like clear cell, papillary and chromophobe, help in the grading of carcinoma on the basis of architectural patterns and nuclear morphology, as well as differentiate benign tumours like oncocytoma from malignant kidney tumours. Similarly, ML algorithms have predicted recurrence risk and survival in RCC [25]. [Table/Fig-6] shows several commercially available AI-based systems and their application in digital pathology [7,26-28].

| AI Platform                                         | Country     | Primary application                | Pathology applications                       | Current regulatory status                |
|-----------------------------------------------------|-------------|------------------------------------|----------------------------------------------|------------------------------------------|
| Paige Prostate Detect                               | USA         | AI-assisted diagnosis              | Prostate cancer                              | FDA De Novo authorised (DEN200080, 2021) |
| Ibex Prostate Detect (formerly Galen™ Second Read™) | Israel      | AI-assisted diagnosis              | Prostate cancer                              | FDA 510(k) cleared (K241232, 2025)       |
| ArteraAI (iQuest)                                   | USA         | Prognosis and treatment prediction | Prostate cancer                              | FDA 510(k) cleared (DEN240068, 2025)     |
| Hologic Genius Digital Diagnostics System           | USA         | AI-assisted cytology screening     | Cervical cytology                            | FDA De Novo authorised (DEN210035, 2024) |
| Lunit INSIGHT DBT                                   | South Korea | AI-assisted diagnosis              | Breast cancer                                | FDA approved                             |
| Aiforia Clinical Suite                              | Finland     | AI-assisted diagnosis              | Histopathology, breast, prostate, biomarkers | CE-IVD certified                         |
| Visiopharm                                          | Denmark     | Image analysis                     | Quantitative pathology, IHC, tissue analysis | CE-marked/ commercial platform           |

**[Table/Fig-6]:** Examples of commercially available Artificial Intelligence (AI) systems in digital pathology and their principal clinical applications. Data compiled from recent literature and regulatory sources [7,26-28].  
AI: Artificial intelligence; FDA: U.S. Food and Drug Administration; CE: Conformité Européenne; IVD: In-vitro Diagnostic Regulation (EU) 2017/746; IHC: Immunohistochemistry

Neuropathology

In neuropathology, AI models support tumour identification, grading, and histological classification of central nervous system tumours including gliomas and medulloblastomas. DL models, including CNNs and transformer-based models has demonstrated accurate classification and grading of glioma subtypes using standard H&E stained sections. These models can predict clinically significant molecular alterations from histological images, such as IDH mutation, MGMT promoter methylation, and 1p/19q co-deletion, thereby providing integrated molecular diagnosis that is in compliance with the WHO classification of CNS tumours [29].

AI has shown potential in the pathology of paediatric brain tumours, particularly medulloblastoma, where ML algorithms can accurately identify and categorise tumour subtypes based on histopathology images [13]. AI models have also been investigated for prognostic prediction, including tumour behaviour and treatment response [30].

Oral Pathology

In oral pathology, AI has been applied to the detection and prognostication of oral cancers, particularly Oral Squamous Cell Carcinoma (OSCC). ML and DL algorithms can help detect architectural and cytological changes like nuclear pleomorphism, increased mitosis, and loss of polarity—all of which are important characteristics in the diagnosis of oral epithelial dysplasia and cancer.

DL models, especially CNNs, have additionally been employed in the detection of keratin pearls and segmentation of epithelial layers, which serve as important histological markers to distinguish among benign, premalignant, and malignant oral lesions.

AI models have also been explored for prognostic prediction, treatment response prediction, recurrence risk, and survival rates in oral malignancies [31].

Haematopathology

In haematopathology, AI has been applied to digital bone marrow analysis, enabling detection and classification of haematopoietic cells and assessment of marrow cellularity. DL models are able to recognise myeloid, erythroid, and megakaryocytic lineages, evaluate the distribution of lineages, and identify subtle morphologic changes and anomalies in haematopoiesis.

Myeloproliferative neoplasms like essential thrombocythemia, polycythemia vera, and primary myelofibrosis have been distinguished using ML-based analysis of megakaryocyte shape and geographic distribution. AI approaches have also been used for detection of dysplasia, grading of fibrosis, and identification of blasts and classifying acute leukaemias in bone marrow specimens [32].

Cutaneous Pathology

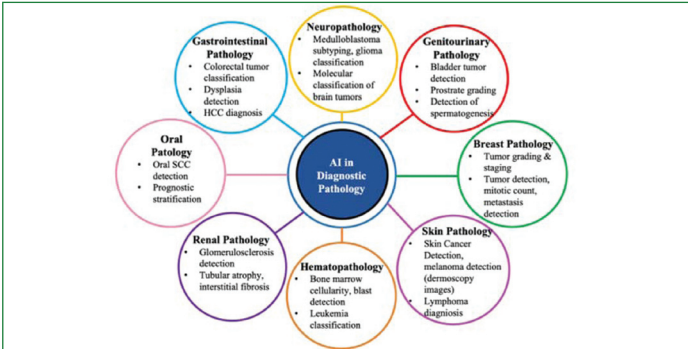
In dermatopathology, AI has been applied to the detection of common skin malignancies, including squamous cell carcinoma, melanoma, and basal cell carcinoma using dermoscopic and histopathological images. AI systems have shown potential in supporting teledermatology and digital triage systems by identifying malignant or premalignant lesions and segregating cases which require prompt expert evaluation [33].

AI models could help reveal potential prognostic biomarkers, differentiate cutaneous lymphomas from reactive infiltrates, and subclassify lymphoma subtypes [34].

[Table/Fig-7] shows the list of key computational tasks in AI-based digital pathology along with the AI methods used and their clinical relevance. [Table/Fig-8] shows radial diagram illustrating organ-wise distribution of AI applications across pathology subspecialties.

| Task                                   | Example AI methods       | Clinical relevance        |
|----------------------------------------|--------------------------|---------------------------|
| Tumour detection                       | CNN, vision transformers | Early diagnosis           |
| Histological classification            | CNN, MIL                 | Tumour subtyping          |
| Tumour grading                         | CNN                      | Prognosis                 |
| Biomarker prediction                   | DL models                | Targeted therapy          |
| Tumour Microenvironment (TME) analysis | U-Net, Graph CNN         | Immunotherapy response    |
| Recurrence prediction                  | ML survival models       | Prognostic stratification |

**[Table/Fig-7]:** Key computational tasks in AI-based digital pathology.  
AI: Artificial intelligence; CNN: Convolutional neural network; MIL: Multiple instance learning; DL: Deep learning; U-Net: Convolutional neural network architecture for image segmentation; ML: Machine learning



**[Table/Fig-8]:** Organ-wise distribution of Artificial Intelligence (AI) applications across pathology subspecialties. The figure illustrates the application of AI in major domains including breast, gastrointestinal, genitourinary, dermatopathology, neuropathology, and Haematopathology.  
AI: Artificial intelligence; SCC: Squamous cell carcinoma; HCC: Hepatocellular carcinoma

## Regulatory and Clinical Implementation

The clinical implementation of AI systems requires rigorous validation, regulatory approval, and incorporation into existing workflows. Standardisation of datasets, external validation, and compliance with regulatory frameworks remain important for safe and effective deployment.

### Challenges

Despite rapid advancements in digital pathology, many practical, regulatory, and technical challenges still limit the widespread clinical adoption of AI systems, and data variability is one of the major challenges. Histological images show marked variation between different labs, which is due to the variations in tissue fixation, staining procedures, slide preparation, and types of slide scanners. When applied to external datasets, this phenomenon— often referred to as ‘domain shift’— can significantly reduce the performance of models trained on data from a single institution. Hence, when AI models trained on the data from one centre are applied to images from another centre, they may limit the generalisability [3].

Additional challenges are algorithm bias and annotation bias. In many studies, model functioning is affected because training datasets are annotated by a limited number of experts, which may bring in subjective labelling errors and noisy annotations. Biased predictions may be produced by AI algorithms if the datasets used for training are small or they are not representative of a wide variety of demographics and illness trends. For dependable model performance, it is consequently crucial to guarantee a variety of large multi-institutional high-quality training datasets with uniform annotations. Moreover, the majority of AI studies in pathology are retrospective, with limited prospective clinical validation. This raises concerns related to real-world applicability and also clinical integration.

Another leading challenge is the computational complexity in the analysis of WSI. For model training and deployment, these extremely large images require substantial memory, processing power, and specialised infrastructure. Because of this, integrating AI systems in standard pathology labs would necessitate a large amount of computational resources and technical assistance [10].

Another big barrier to clinical implementation is the regulatory validation and approval. AI-based diagnostic tools must undergo stringent clinical validation and regulatory evaluation procedure before they are used in clinical settings so as to guarantee their safety and reliability. However, in pathology, the safety regulations for AI are still developing, which may impede its clinical application.

Lastly, ethical issues, which include patient data privacy, algorithm transparency, and potential over-reliance on automated systems, need to be carefully considered. It is challenging to justify how predictions are made as many DL models function as “black box” systems, which can limit clinical trust and acceptance. XAI approaches aim to enhance transparency by highlighting regions of interest and histological features that affect model predictions. This helps in providing interpretable decision pathways, thereby facilitating clinical confidence and helping regulatory acceptance [6,10,27].

Thus, AI should be seen as a decision-support tool rather than a replacement for pathologist expertise. In spite of these drawbacks, current advances in computational methodologies, foundation models, and multimodal learning have continued to widen the potential uses in clinical settings of AI in pathology [2].

## Future Directions of Artificial Intelligence (AI) in Pathology

**Foundation Models, Precision Medicine and Multimodal AI:** Recent advances in foundation models trained on large-scale datasets have enabled cross-domain learning in pathology. Integration of histology images with genomic, radiologic, and clinical

data through multimodal AI is expected to enhance precision diagnostics and personalised treatment strategies. By facilitating more precise patient stratification and individualised treatment plans, such integrative techniques may improve tumour detection, grading, categorisation, predict molecular changes, and enable precision oncology [9,10].

In the coming years, foundation models are expected to improve diagnostic accuracy, particularly for uncommon tumours and histological variants for which annotated datasets are scarce. Moreover, generative AI techniques could assist in data augmentation, virtual staining, and simulation-based training, which would enhance the robustness of the models. Another promising method is federated learning, which can facilitate collaborative model training across multiple institutions without sharing patient-level data. This would improve data privacy, model generalisability and multicentre validation [10].

## Regulatory Approval and Clinical Translation

To achieve successful clinical application, AI systems in pathology must undergo thorough validation through prospective studies across multiple institutions. The establishment of standardised regulatory frameworks and clear pathways for approval is crucial to ensure that AI tools are safe, reliable, and reproducible in everyday practice.

Future initiatives should prioritise the incorporation of AI systems into current laboratory workflows, the creation of user-friendly interfaces, and the compatibility with digital pathology platforms. Collaborative efforts among clinicians, pathologists, and regulatory bodies will be essential for transitioning AI innovations into practical clinical use.

### Limitation(s)

The literature search was mainly performed with PubMed and Google Scholar and could have missed some relevant studies indexed in other databases. This is a narrative review, no formal systematic review methods or quantitative meta-analyses were performed. Moreover, the field of AI in pathology is rapidly evolving and some newly published developments may not have been included. Despite these limitations, this review provides a comprehensive overview of current applications, challenges and future directions of AI in diagnostic pathology.

## CONCLUSION(S)

The AI is rapidly transforming the field of diagnostic pathology via advances in digital pathology, DL, and digital image analysis. AI algorithms have shown promising results across various subspecialties, including breast, gastrointestinal, neuropathology, genitourinary, haematopathology, oral pathology, and dermatopathology, in functions like tumour detection, classification, and biomarker prediction. Although for successful clinical adoption, diligent integration with pathologists’ knowledge, regulatory oversight, and strong validation across multiple datasets are required. AI is expected to serve as a powerful decision-support tool rather than to replace pathologists. Hence, AI should be incorporated as a human–AI collaborative system where pathologists hold the ultimate diagnostic responsibility while leveraging AI for decision support.

Future research must focus on large standardised datasets, multimodal data integration, and real-world clinical validation to achieve the full potential of AI-based precision pathology, and improve patient outcomes.

**Use of Artificial Intelligence (AI) Tools/Disclosure:** AI-assisted design tools were used to generate conceptual diagrams included in this manuscript. All images were manually reviewed and edited by the authors, who are responsible for the accuracy and integrity of the content.

## REFERENCES

- [1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024;74(3):229-63. Doi: 10.3322/caac.21834.
- [2] Sagiv C, Hadar O, Najjar A, Pahnke J. Artificial intelligence in surgical pathology - where do we stand, where do we go? *Eur J Surg Oncol.* 2025;51(7):109541. Doi: 10.1016/j.ejso.2024.109541.
- [3] Marra A, Morganti S, Pareja F, Campanella G, Bibeau F, Fuchs T, et al. Artificial intelligence entering the pathology arena in oncology: current applications and future perspectives. *Ann Oncol.* 2025;36(7):712-25. Doi: 10.1016/j.annonc.2025.03.006.
- [4] Shaktah LA, Carrero ZI, Hewitt KJ, Gustav M, Cecchini M, Foersch S, et al. Application of artificial intelligence and digital tools in cancer pathology. *Lancet Digit Health.* 2025;7(10):100933. Doi: 10.1016/j.landig.2025.100933.
- [5] Jariyapan P, Pora W, Kasamsunran N, Lekawanvijit S. Digital pathology and artificial intelligence in diagnostic pathology. *Malays J Pathol.* 2025;47(1):3-12.
- [6] Zhang DY, Venkat A, Khasawneh H, Sali R, Zhang V, Pei Z. Implementation of digital pathology and artificial intelligence in routine pathology practice. *Lab Invest.* 2024;104(9):102111. Doi: 10.1016/j.labinv.2024.102111.
- [7] Berezowska S, Cathomas G, Grobholz R, Henkel M, Jochum W, Koelzer VH, et al. Digital image analysis and artificial intelligence in pathology diagnostics - the Swiss view. *Pathologie (Heidelb).* 2023;44(Suppl 3):222-24. Doi: 10.1007/s00292-023-01262-w.
- [8] Shafi S, Parwani AV. Artificial intelligence in diagnostic pathology. *Diagn Pathol.* 2023;18(1):109. Doi: 10.1186/s13000-023-01375-z.
- [9] Waqas A, Bui MM, Glassy EF, El Naqa I, Borkowski P, Borkowski AA, et al. Revolutionizing digital pathology with the power of generative artificial intelligence and foundation models. *Lab Invest.* 2023;103(11):100255. Doi: 10.1016/j.labinv.2023.100255.
- [10] Zhang X, Gao T, Cai Q, Xia J, Sun Y, Yang J, et al. Artificial intelligence in digital pathology diagnosis and analysis: technologies, challenges, and future prospects. *Mil Med Res.* 2025;12(1):93. Doi: 10.1186/s40779-025-00680-6.
- [11] Bai B, Yang X, Li Y, Zhang Y, Pillar N, Ozcan A. Deep learning-enabled virtual histological staining of biological samples. *Light Sci Appl.* 2023;12:57. <https://doi.org/10.1038/s41377-023-01104-7>.
- [12] Klöckner P, Teixeira J, Montezuma D, Fraga J, Horlings HM, Cardoso JS, et al. H&E to IHC virtual staining methods in breast cancer: an overview and benchmarking. *NPJ Digit Med.* 2025;8(1):384. <https://doi.org/10.1038/s41746-025-01741-9>.
- [13] Alzoubi H, Abd-Alrazaq A, Almaabreh O, AlSaad R, Aziz S, Al-Dafi R, et al. Diagnostic performance of artificial intelligence in detecting and subtyping pediatric medulloblastoma from histopathological images: A systematic review. *Artif Intell Med.* 2025;169:103237. Doi: 10.1016/j.artmed.2025.103237.
- [14] Salehi MA, Harandi H, Mohammadi S, Shahrabi Farahani M, Shojaei S, Saleh RR. Diagnostic performance of artificial intelligence in detection of hepatocellular carcinoma: A meta-analysis. *J Imaging Inform Med.* 2024;37(4):1297-311. Doi: 10.1007/s10278-024-01058-1.
- [15] Egevad L, Camilloni A, Delahunt B, Samaratunga H, Eklund M, Kartasalo K. The role of artificial intelligence in the evaluation of prostate pathology. *Pathol Int.* 2025;75(5):213-20. Doi: 10.1111/pin.70015.
- [16] Liu Y, Han D, Parwani AV, Li Z. Applications of artificial intelligence in breast pathology. *Arch Pathol Lab Med.* 2023;147(9):1003-13. Doi: 10.5858/arpa.2022-0457-RA.
- [17] Datwani S, Khan H, Khan Niazi MK, Parwani AV, Li Z. Artificial intelligence in breast pathology: overview and recent updates. *Hum Pathol.* 2025;162:105819. Doi: 10.1016/j.humpath.2025.105819.
- [18] Kim KO, Kim EY. Application of artificial intelligence in the detection and characterization of colorectal neoplasm. *Gut Liver.* 2021;15(3):346-53. Doi: 10.5009/gnl20186.
- [19] Kuntz S, Krieghoff-Henning E, Kather JN, Jutzi T, Höhn J, Kiehl L, et al. Gastrointestinal cancer classification and prognostication from histology using deep learning: systematic review. *Eur J Cancer.* 2021;155:200-15. Doi: 10.1016/j.ejca.2021.07.012.
- [20] Chuluunbaatar Y, Bansal S, Brodie A, Sharma A, Vasdev N. The current use of artificial intelligence in testicular cancer: a systematic review. *Artif Intell Surg.* 2023;3:195-206. Doi: 10.20517/ais.2023.26.
- [21] Patel AU, Parwani AV, Satturwar S. Artificial intelligence in genitourinary pathology. *Histopathology.* 2026;88(1):353-73. Doi: 10.1111/his.70020.
- [22] Hsu CH, Yeh CF, Huang IS, Chen WJ, Peng YC, Tsai CH, et al. Artificial intelligence interpretation of touch print smear cytology of testicular specimen from patients with azoospermia. *J Assist Reprod Genet.* 2024;41(11):3179-87. Doi: 10.1007/s10815-024-03215-5.
- [23] Ferro M, Falagario UG, Barone B, Maggi M, Crocetto F, Busetto GM, et al. Artificial intelligence in the advanced diagnosis of bladder cancer - comprehensive literature review and future advancement. *Diagnostics (Basel).* 2023;13(13):2308. Doi: 10.3390/diagnostics13132308.
- [24] Feng C, Liu F. Artificial intelligence in renal pathology: current status and future. *Biomol Biomed.* 2023;23(2):225-34. Doi: 10.17305/bjbm.2022.8318.
- [25] Walsh D, Hayes C. Using artificial intelligence to advance renal cancer diagnosis, treatment, and precision medicine. *Ann Urol Oncol.* 2025;8(2):01-09. Doi: 10.32948/aao.2025.08.20.
- [26] Bulten W, Kartasalo K, Chen PC, Ström P, Pinckaers H, Nagpal K, et al. Artificial intelligence for diagnosis and Gleason grading of prostate cancer: The PANDA challenge. *Nat Med.* 2022;28(1):154-63. Doi: 10.1038/s41591-021-01620-2.
- [27] Bera K, Schalper KA, Rimm DL, Velcheti V, Madabhushi A. Artificial intelligence in digital pathology - new tools for diagnosis and precision oncology. *Nat Rev Clin Oncol.* 2019;16(11):703-15. Doi: 10.1038/s41571-019-0252-y.
- [28] U.S. Food and Drug Administration. Artificial intelligence-enabled medical devices [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; [cited 2026 Jul 1]. Available from: <https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-enabled-medical-devices>
- [29] Sakaguchi M, Yoshizawa A, Masui K, Sakai T, Komori T. AI-powered histology for molecular profiling in brain tumours: toward smart diagnostics from tissue. *Cancers (Basel).* 2025;18(1):9. Doi: 10.3390/cancers18010009.
- [30] Redlich JP, Feuerhake F, Weis J, Schaadt NS, Teuber-Hanselmann S, Buck C, et al. Applications of artificial intelligence in the analysis of histopathology images of gliomas: A review. *NPJ Imaging.* 2024;2(1):16. Doi: 10.1038/s44303-024-00020-8.
- [31] Krishna AB, Tanveer A, Bhagirath PV, Gannepalli A. Role of artificial intelligence in diagnostic oral pathology- A modern approach. *J Oral Maxillofac Pathol.* 2020;24(1):152-56. Doi: 10.4103/jomfp.JOMFP\_215\_19.
- [32] van Eekelen L, Litjens G, Hebeda KM. Artificial intelligence in bone marrow histological diagnostics: Potential applications and challenges. *Pathobiology.* 2024;91(1):08-17. Doi: 10.1159/000529701.
- [33] Giavina-Bianchi M, Ko J. Editorial: artificial intelligence in cutaneous lesions: where do we stand and what is next? *Front Med (Lausanne).* 2024;11:1420152. Doi: 10.3389/fmed.2024.1420152.
- [34] Doleman T, Hondelink LM, Vermeer MH, van Dijk MR, Schrader AMR. Artificial intelligence in digital pathology of cutaneous lymphomas: a review of the current state and future perspectives. *Semin Cancer Biol.* 2023;94:81-88. Doi: 10.1016/j.semcancer.2023.06.004.

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