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Review Article

Role of artificial intelligence in histopathological diagnosis of cancer current status and future directions

Trushali Mandhare[1]*, Pooja Kashid[1], Devata Shinde[2], Pankaj Khuspe[2], Ritesh Digambar Vyavahare[3]

[1]Dept. of Pharmacy, Navsahyadri Institute of Pharmacy, Nasrapur, Maharashtra, India
[2]Dept. of Pharmacy, Shriram Shikshan Sanstha's College of Pharmacy, Paniv, Maharashtra, India
[3]Dept. of Pharmaceutics, SVERI's College of Pharmacy, Pandharpur, Maharashtra, India

Abstract

Histopathological diagnosis remains the cornerstone of cancer detection, classification, and prognostication. However, conventional approaches are often challenged by inter-observer variability, workload burden, and the growing complexity of oncological pathology. Recent advances in artificial intelligence (AI), particularly machine learning (ML) and deep learning (DL), have introduced transformative opportunities for digital pathology. AI-enabled algorithms have demonstrated remarkable accuracy in tasks such as tumor detection, grading, subtyping, and prediction of molecular alterations directly from histology slides. Whole-slide imaging (WSI), coupled with convolutional neural networks (CNNs), has enabled automated quantification of morphological patterns, mitotic figures, and tumor–stroma interactions with precision comparable to expert pathologists. Furthermore, AI systems are increasingly being integrated into prognostic and predictive frameworks, facilitating personalized medicine through the correlation of histopathological features with clinical outcomes and therapeutic responses. Despite this progress, several limitations hinder widespread adoption, including variability in data quality, lack of standardized validation, interpretability challenges, and regulatory concerns. Moreover, integration into clinical workflows demands rigorous evaluation of algorithmic transparency, generalizability across populations, and acceptance by pathologists. This review critically examines the current landscape of AI in histopathological cancer diagnosis, highlighting state-of-the-art applications, translational challenges, and emerging trends. Emphasis is placed on the potential synergy between human expertise and AI-driven decision support, which may reshape the future of oncological pathology. Ultimately, AI holds the promise of augmenting diagnostic accuracy, reducing workload, and enabling precision oncology, provided that ethical, technical, and implementation barriers are systematically addressed.

Keywords: Artificial intelligence, Histopathology, Cancer diagnosis, Digital pathology, Deep learning.

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1. Introduction

Cancer represents one of the leading global health burdens, accounting for nearly 20 million new cases and approximately 10 million deaths annually, with incidence projected to rise markedly in the coming decades. Early and accurate diagnosis remains pivotal to effective treatment planning, prognostication, and implementation of precision oncology strategies. Among the available diagnostic modalities, histopathological evaluation constitutes the gold standard for cancer detection and characterization. Microscopic assessment of tissue architecture and cellular morphology allows pathologists to classify tumors by type, grade, and stage, and, when combined with ancillary techniques such as immunohistochemistry (IHC), fluorescence in situ hybridization (FISH), and next-generation sequencing (NGS), provides critical molecular and prognostic insights.[1,2]

Despite its indispensability, conventional/manual histopathology faces inherent constraints. Diagnostic accuracy is limited by inter-observer variability, particularly

*Corresponding author: Trushali Mandhare
Email: khuspepankaj@gmail.com

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in borderline or morphologically heterogeneous lesions. The growing complexity of oncological classification systems, together with the escalating global cancer burden, contributes to substantial workload pressures, often resulting in delayed reporting and inconsistent interpretation across institutions. Traditional computational methods, including rule-based image analysis and handcrafted feature extraction, have attempted to address some of these challenges. While useful for quantifying nuclear morphology, mitotic activity, or biomarker expression, these approaches are vulnerable to staining variability, artifacts, and tumor heterogeneity, restricting their reproducibility and clinical translation.[3]

The advent of WSI and digital pathology has created a foundation for computational pathology, within which AI has emerged as a transformative tool. DL architectures such as CNNs and transformer-based models can autonomously extract hierarchical features from large-scale histological datasets. This enables robust discrimination between normal and malignant tissue, accurate tumor subtyping, grading, and even prediction of underlying genomic alterations directly from hematoxylin and eosin (H&E) slides. AI-driven systems offer clear advantages: reduction of observer-related subjectivity, improved reproducibility, heightened sensitivity to subtle histomorphological cues, and scalability for high-volume workflows. Moreover, AI facilitates integration of morphological, molecular, and clinical data, thereby expanding the scope of precision oncology.[4]

Nonetheless, several barriers persist, including data heterogeneity, scarcity of large annotated datasets, limited interpretability of algorithms, and regulatory considerations. Addressing these challenges requires close collaboration between computational scientists, pathologists, and regulatory bodies. This review critically examines the role of AI in histopathological diagnosis of cancer, focusing on current applications, existing limitations, and future directions. Particular emphasis is placed on how synergistic integration of AI-based algorithms with expert pathology practice may redefine diagnostic paradigms and accelerate the translation of computational pathology into routine clinical care.[5]

2. Fundamentals of Artificial Intelligence in Histopathology

2.1. Overview of artificial intelligence, machine learning, and deep learning

AI in pathology represents a paradigm shift from human-dependent interpretation to computational augmentation of diagnostic workflows. ML, traditionally based on algorithms such as support vector machines (SVMs), random forests, and k-nearest neighbors (k-NN), has long been applied to biomedical imaging. However, these methods relied heavily on handcrafted features—such as nuclear size, shape descriptors, and texture parameters—which were prone to bias and lacked adaptability to highly heterogeneous histological landscapes.[6]

DL overcomes these constraints by employing multi-layered neural networks capable of hierarchical feature learning. CNNs in particular, have demonstrated state-of-the-art performance in histopathology, achieving classification accuracies exceeding 95% in certain benchmark datasets such as The Cancer Genome Atlas (TCGA). Recent innovations, including Vision Transformers (ViTs) and graph neural networks (GNNs), allow models to capture long-range dependencies and spatial tissue architecture beyond local patch-level analysis, further improving contextual understanding.[7]

2.2. Whole-slide imaging and the digitization of pathology

WSI is the enabling technology for computational histopathology. By converting glass slides into gigapixel-scale digital images, WSI facilitates both telepathology and large-scale algorithm training. Current high-throughput scanners operate at 20× to 40× magnification, generating files often exceeding several gigabytes per slide. The adoption of WSI has expanded rapidly; in certain pathology centers, over 90% of diagnostic workflows are now digitized, with regulatory approvals (e.g., FDA clearance of WSI for primary diagnosis in 2017) accelerating clinical integration. However, challenges persist: variations in scanner hardware, staining protocols, and slide preparation introduce batch effects that can confound AI performance. Harmonization techniques, such as stain normalization using generative adversarial networks (GANs), are increasingly applied to reduce these sources of variability.[8]

2.3. Convolutional neural networks and key architectures

CNNs remain the backbone of AI-driven histopathology. They operate through convolutional layers that extract spatially localized features, pooling layers that reduce dimensionality, and fully connected layers that integrate learned representations. Architectures such as ResNet (residual networks) address vanishing gradient problems in deep architectures, Inception models leverage multi-scale filters for capturing diverse morphological features, while DenseNet enhances feature propagation through dense connectivity.[9] Notably, CNN-based approaches have demonstrated clinical potential. For example, AI systems trained on WSIs from breast cancer biopsies have achieved sensitivity and specificity exceeding 90% in detecting invasive carcinoma, often outperforming junior pathologists. Similarly, in prostate cancer, DL algorithms have reached concordance rates with expert pathologists of up to 98% in Gleason grading tasks. More advanced models, including ViTs, process entire WSI patches with global attention mechanisms, offering improved interpretability and performance in complex cancers such as gliomas and gastric adenocarcinomas. Hybrid architectures integrating CNNs with GNNs are being explored to model spatial relationships between cells and tissue compartments, capturing tumor–immune microenvironment interactions that are highly relevant for predicting therapeutic response.[10]

2.4. AI Training pipelines: annotation, feature extraction, and validation

2.4.1. Robust AI development requires carefully curated training pipelines.

Annotation: Pathologists generate ground-truth labels by delineating tumor regions, mitotic hotspots, or immune infiltrates. This step is resource-intensive; annotating a single WSI may require several hours. Emerging strategies, such as weakly supervised learning and multiple-instance learning, reduce dependency on exhaustive manual annotation by leveraging slide-level labels.[11] Feature Extraction: CNNs or ViTs automatically learn discriminative features directly from pixel data. Transfer learning using pretrained networks on large image datasets (e.g., ImageNet) before fine-tuning on histopathology—accelerates convergence and reduces the need for extremely large domain-specific datasets.[12]

Validation: Rigorous evaluation is essential to prevent overfitting. Internal validation typically employs stratified k-fold cross-validation, while external validation across multi-institutional cohorts ensures generalizability. For example, AI models for colorectal cancer classification trained on TCGA have achieved area under the curve (AUC) values above 0.95 when externally validated on independent cohorts. However, performance often drops significantly when applied to real-world clinical datasets, underscoring the importance of external benchmarking.[13]

Performance Metrics: Beyond accuracy, evaluation relies on sensitivity, specificity, AUC, and F1-score. Calibration curves and decision-curve analyses are increasingly recommended to assess clinical utility. Regulatory-grade validation may also require demonstration of non-inferiority compared with expert human performance.[14]

The integration of WSI, advanced neural architectures, and carefully constructed training-validation pipelines has laid a robust foundation for AI in histopathology. Quantitative evidence from multiple cancer types demonstrates AI's capability to match or exceed human-level performance in diagnostic classification, grading, and molecular prediction. However, real-world implementation demands solutions to challenges such as dataset heterogeneity, interpretability, and integration into clinical workflows. The convergence of AI with multi-omics, federated learning, and explainable AI (XAI) is expected to further enhance reliability and acceptance, marking a decisive step toward routine computational pathology in cancer diagnostics.[15]

3. Current Applications of AI in Cancer Histopathology

3.1. Tumor detection and classification

Automated tumor detection is one of the most extensively validated applications of AI in histopathology. CNNs and transformer-based models have achieved high accuracy in distinguishing malignant from benign tissue across diverse tumor types. For example, in breast pathology, AI systems trained on large-scale datasets have demonstrated diagnostic accuracies exceeding 95% in detecting invasive carcinoma, sometimes surpassing general pathologists in sensitivity. In lung cancer, algorithms can reliably differentiate between adenocarcinoma and squamous cell carcinoma, achieving performance comparable to thoracic pathology specialists. Similarly, AI applications in prostate biopsies have reached near-perfect agreement with expert pathologists in detecting microfoci of carcinoma, reducing the likelihood of missed diagnoses in small-volume disease. These findings suggest that AI-based classification could serve as a valuable triage tool, flagging suspicious cases for priority review and thereby improving diagnostic throughput.[16]

3.2. Grading and staging

Tumor grading, which evaluates morphological hallmarks such as mitotic activity, nuclear atypia, and tissue architecture, is central to prognostication but highly vulnerable to inter-observer variability. AI models have shown strong promise in addressing this limitation. Automated mitotic figure detection, for instance, has reached sensitivities above 90%, outperforming manual counts that are often inconsistent due to sampling bias and observer fatigue. In prostate cancer, AI-assisted Gleason grading has demonstrated concordance rates of 95–98% with expert uropathologists, substantially higher than the agreement observed among general pathologists. Similarly, in breast carcinoma, DL-based models trained on thousands of slides have improved reproducibility of Nottingham grading by standardizing quantification of nuclear pleomorphism and glandular differentiation. Emerging studies also suggest that AI can assist in early-stage tumor staging by identifying subtle patterns of invasion, lymphovascular spread, or micrometastases in lymph nodes that may be overlooked by human observers.[17]

3.3. Prognostic and predictive modeling

Beyond diagnosis, AI is increasingly being leveraged for prognostic and predictive tasks. By quantifying morphological features of the tumor microenvironment including stromal composition, immune infiltration, and angiogenic patterns AI systems can stratify patients into high- or low-risk categories for recurrence and survival. For example, DL models analyzing digitized colorectal cancer slides have been able to predict 5-year disease-free survival with performance metrics comparable to established clinical staging systems. In breast cancer, AI-driven quantification of tumor-infiltrating lymphocytes has emerged as a reliable biomarker of response to immunotherapy. Importantly, predictive modeling is not limited to conventional histology: integration of digital pathology with treatment response data has enabled algorithms to forecast outcomes of chemotherapy, targeted therapy, and immunotherapy with growing accuracy. This capability positions AI as a central tool for advancing precision medicine by tailoring treatment strategies to histomorphological biomarkers.[18]

3.4. Molecular and genomic correlates

One of the most disruptive applications of AI in histopathology is the prediction of molecular and genomic alterations directly from hematoxylin and eosin (H&E)-stained slides. Pioneering studies have demonstrated that CNNs trained on TCGA datasets can accurately predict isocitrate dehydrogenase (IDH) mutation status in gliomas, epidermal growth factor receptor (EGFR) mutations in lung adenocarcinoma, and KRAS or TP53 mutations in colorectal carcinoma, with AUC values frequently exceeding 0.85. Such models bypass the need for costly and time-intensive molecular assays, potentially enabling rapid and resource-efficient patient stratification, especially in low-resource settings. AI has been applied to predict microsatellite instability (MSI) and tumor mutational burden (TMB) both critical biomarkers for immunotherapy response directly from histology, with accuracy approaching that of molecular gold standards. While not yet ready to replace genomic sequencing, these approaches highlight AI's potential to bridge histology and genomics, thereby redefining the boundaries of digital pathology.[19]

3.5. Workflow optimization

The utility of AI extends beyond diagnostic accuracy to practical workflow enhancements. AI-assisted triage systems can pre-screen large volumes of slides, automatically highlighting regions of interest (ROIs) or ranking cases based on likelihood of malignancy, thus reducing turnaround times. In high-volume cancer centers, such systems have already demonstrated reductions in pathologist review time by up to 50%. Moreover, automated quantification of IHC and in situ hybridization assays has become increasingly reliable.[20]

AI-based scoring systems for biomarkers such as HER2, Ki-67, and PD-L1 have shown concordance rates exceeding 90% with expert manual scoring, while offering improved reproducibility and scalability. These advances not only enhance efficiency but also reduce the risk of human error in borderline or equivocal cases. Integration of AI with laboratory information systems (LIS) and digital workflows further supports real-time reporting and quality control, advancing the transition toward fully digital, AI-augmented pathology laboratories. AI applications in histopathology have rapidly expanded from tumor detection and grading to prognostic modeling, genomic prediction, and workflow optimization. While still in the translational phase, accumulating evidence demonstrates that AI systems can match or exceed expert-level performance in multiple diagnostic and predictive tasks. The convergence of diagnostic precision, prognostic insights, and efficiency gains underscores the transformative potential of AI in cancer histopathology, paving the way for integration into routine clinical workflows.[21,22]

Table 1: Current applications of AI in histopathological diagnosis of cancer[12-21]

Application	AI Methodologies Commonly Used	Key Outcomes	Advantages	Limitations/Challenges
Tumor Detection & Classification	CNNs, Vision Transformers	Distinguish malignant vs. benign; subtype cancers (breast, lung, prostate)	High sensitivity, automated screening	Staining variability, domain shift
Grading & Staging	Deep CNNs, Patch-based analysis	Automated mitotic count, nuclear atypia, architectural grading	Improved reproducibility, reduced observer bias	Requires large annotated datasets
Prognostic & Predictive Modeling	Multi-modal DL, Survival models	Correlation of morphology with outcomes; prediction of therapy response	Enables risk stratification, personalized medicine	Lack of external validation
Molecular/Genomic Prediction	CNNs with WSI-to-genomics mapping	Predict IDH, EGFR, KRAS, MSI from H&E	Cost-effective surrogate for sequencing	Lower accuracy in rare mutations
Workflow Optimization	Weakly supervised DL, AI triage tools	Prioritization of high-volume cases; automated IHC quantification	Reduced workload, faster turnaround	Integration into existing LIS workflows is challenging

Table 2: Comparative overview of traditional vs. AI-augmented histopathology[22-26]

Parameter	Traditional/Manual Histopathology	AI-Augmented Histopathology	Evidence/Reported Data
Diagnostic Accuracy	Dependent on pathologist expertise; inter-observer variability up to 30–40% (e.g., breast, prostate cancer grading).	CNN/DL models achieve >95% concordance with experts; outperform average pathologists in challenges.	CAMELYON16: AI AUC 0.994 for metastasis detection.
Reproducibility	Variable across institutions; affected by training and workload.	High reproducibility with standardized algorithms; consistency across datasets.	Multi-center studies show stable AI performance despite staining variation.
Turnaround Time	Manual review requires hours per case series; bottleneck in high-volume settings.	AI triage reduces workload by 40–60%; pathologist review time cut from 120 → 45 minutes in breast cancer lymph node cases.	Clinical workflow studies.
Detection of Subtle Features	Limited by human perception; mitotic count sensitivity <70%.	AI achieves >90% sensitivity in mitotic figure detection; identifies micrometastases <0.2 mm.	DL-based detection studies.
IHC/Biomarker Quantification	Manual scoring subject to variability; inter-rater correlation often <0.85.	Automated quantification with correlation >0.95 to expert scoring; standardized PD-L1, Ki-67, ER/PR assessments.	Validation studies on IHC.
Molecular Prediction from H&E	Requires additional assays (IHC, FISH, NGS); expensive and time-consuming.	Predicts IDH1/2, EGFR, KRAS, MSI directly from histology with AUC 0.85–0.95.	Recent AI-genomic correlation models.
Scalability	Workforce-limited; pathologist shortage projected worldwide.	Scalable across high-volume digital pathology platforms; enables global deployment.	WHO workforce reports + AI deployment case studies.

4. Advantages of AI Integration in Histopathology

4.1. Improved accuracy and reproducibility

Reproducibility remains a critical challenge in diagnostic pathology. Inter-observer variability in cancer grading can reach up to 30–40% in breast carcinoma and 20–25% in prostate Gleason scoring, leading to discordance in treatment recommendations. AI-based systems, particularly CNNs, trained on datasets exceeding 100,000 whole-slide images (WSIs), have consistently demonstrated concordance with expert pathologists at levels surpassing 95% agreement, which is higher than consensus among trained pathologists themselves. In the CAMELYON16 challenge, AI algorithms achieved an AUC of 0.994 for detecting lymph node metastases, outperforming the average pathologist sensitivity. These data underscore the potential of AI to standardize histopathological interpretations globally, particularly across centers with varying levels of diagnostic expertise.[23]

4.2. Reduction in workload and turnaround time

The global cancer burden, projected to exceed 28 million new cases annually by 2040, intensifies pressure on pathology services already constrained by workforce shortages. AI-enabled triage systems can pre-screen WSIs and prioritize suspicious cases, reducing manual review time by 40–60% without loss of accuracy. In breast cancer lymph node evaluation, for example, automated pre-screening reduced average pathologist assessment time from 120 minutes to 45 minutes per case series. Moreover, AI-driven IHC quantification has been shown to produce consistent PD-L1 scoring with a correlation coefficient of >0.95 compared to expert manual scoring, eliminating subjective inconsistencies while accelerating reporting. These reductions in turnaround time are clinically significant, as delays of even 5–7 days in diagnosis have been associated with measurable declines in patient outcomes in aggressive cancers.[24]

4.3. Enhanced detection of subtle morphological features

Human perception is inherently constrained, particularly in detecting rare or subtle morphological features. AI, however, excels at extracting high-dimensional features invisible to manual review. For instance, DL algorithms have demonstrated sensitivity >90% in mitotic figure detection, compared to <70% for human experts in time-limited settings. In colorectal cancer, AI has been shown to detect micrometastases <0.2 mm, which are often overlooked in manual screening. Furthermore, computational models capture stromal remodeling, tumor–immune spatial distribution, and nuclear textural features that correlate strongly with patient survival but remain underutilized in routine pathology. These capabilities extend histopathology from a purely diagnostic modality toward a quantitative biomarker discovery platform.[25]

4.4. Support for precision oncology and personalized treatment

AI facilitates integration of histomorphology with molecular and clinical outcomes, serving as a cost-effective complement to NGS. Emerging evidence demonstrates that CNN-based models can predict IDH1/2 mutation status in gliomas with >90% accuracy, EGFR mutations in non-small-cell lung cancer with AUC ~0.85, and microsatellite instability in colorectal cancer with accuracy >88%, all from H&E images alone. Such predictive capacity enables stratification of patients for targeted therapy or immunotherapy, even in low-resource settings where molecular testing is limited. Additionally, AI-derived tumor microenvironment features, such as quantification of CD8+ T-cell infiltration or tertiary lymphoid structures, have been correlated with immunotherapy response, providing predictive biomarkers that complement conventional assays. Together, these applications position AI as a key enabler of precision oncology.[26]

The integration of AI into histopathology offers measurable improvements across diagnostic accuracy, efficiency, feature sensitivity, and translational relevance. By reducing inter-observer variability, accelerating case triage, uncovering subtle features, and predicting molecular phenotypes, AI enhances both the reliability and scope of histopathological practice. Importantly, these tools function not as replacements for human expertise but as force multipliers that expand diagnostic capacity in an era of escalating cancer incidence. The synergy of computational algorithms and expert pathology interpretation promises to usher in a new standard of reproducibility, efficiency, and personalization in oncological care.[27]

5. Challenges and Limitations

5.1. Variability in slide preparation and data quality

AI algorithms are highly sensitive to pre-analytical and analytical variations inherent in histopathological workflows. Studies have demonstrated that differences in fixation (formalin vs. alcohol-based), embedding, section thickness, and H&E staining intensity can introduce color and texture variability that significantly degrade model performance. For example, CNN-based models trained on slides from a single institution often experience 20–30% drops in accuracy when applied to external cohorts due to staining heterogeneity. Computational strategies such as stain normalization, domain adaptation, and GANs have been explored to mitigate these effects, yet robust cross-institutional standardization remains an unsolved challenge. Furthermore, technical artifacts including tissue folds, necrosis, crush injury, or scanning resolution mismatch contribute additional noise, lowering the reproducibility of AI outputs.[28]

5.2. Lack of standardized datasets and external validation

Most published AI pathology models rely on single-institution datasets of limited size (often <1000 patients), raising concerns of over fitting and poor generalizability. While benchmark repositories such as TCGA and CAMELYON16/17 datasets have enabled proof-of-concept studies, they represent selective subsets of tumor types and lack representation of ethnically and geographically diverse populations. Moreover, only a minority of algorithms undergo rigorous external validation across independent, multi-center cohorts, which is considered a gold standard for regulatory approval. The absence of large-scale, harmonized, and annotated datasets akin to those available in radiology is a major bottleneck limiting clinical translation.[29]

5.3. Algorithm interpretability and "Black-Box" concerns

DL models, particularly CNNs and transformer architectures, achieve AUCs exceeding 0.95 for specific cancer classification tasks; however, they often provide no explicit reasoning behind predictions. This "black-box" nature undermines clinical accountability and medico-legal defensibility. For instance, an AI system may accurately classify lung adenocarcinoma but cannot explain whether its decision was based on nuclear pleomorphism, glandular architecture, or stromal reaction. Emerging frameworks in XAI, such as class activation maps, Grad-CAM, and attention-based heatmaps, attempt to highlight morphological features driving predictions. Nevertheless, these methods remain semi-quantitative, lack consensus validation, and may introduce new interpretive ambiguities, limiting trust among pathologists and regulators.[30]

5.4. Ethical, regulatory, and legal barriers

The integration of AI into clinical oncology raises ethical and regulatory complexities. Patient consent and privacy during dataset aggregation remain contentious, particularly in light of the GDPR in Europe and HIPAA in the United States. Algorithmic bias, arising from underrepresentation of minority populations in training data, risks amplifying diagnostic disparities. For example, recent analyses have shown reduced AI accuracy in underrepresented ethnic cohorts for breast and skin cancer histology. Regulatory pathways are also fragmented: while the FDA has approved AI-based radiology tools, approvals for histopathology remain rare due to the higher variability of tissue samples. Moreover, liability in cases of AI-assisted misdiagnosis remains unresolved, raising medico-legal uncertainty for practicing pathologists.[31]

5.5. Pathologist acceptance and workforce integration

Although AI is positioned as an augmentative rather than replacement technology, surveys reveal persistent skepticism among pathologists. Concerns include diagnostic deskilling, overreliance on algorithms, and conflicts in cases of human AI disagreement. Importantly, medico-legal accountability ultimately resides with the pathologist, making them cautious in adopting opaque AI tools. Successful integration requires transparent clinical validation, intuitive user interfaces, and educational initiatives to train pathologists in computational literacy. Early pilot studies have shown that AI-assisted workflows can reduce case review time by 20–40%, particularly in prostate and breast cancer screening, but broader acceptance depends on demonstrable real-world impact without compromising diagnostic autonomy.[32]

6. Future Directions

The trajectory of AI in histopathological oncology is defined by the dual imperatives of scientific rigor and translational scalability. Although existing applications have demonstrated proof-of-concept efficacy, real-world adoption will depend on advances in explainability, generalizability, multimodal integration, and deployment frameworks that balance automation with human oversight.[33]

6.1. Explainable AI and interpretable models

One of the foremost challenges is the limited interpretability of DL systems, which operate as high-dimensional "black-boxes." In diagnostic oncology, where clinical accountability and medico-legal defensibility are paramount, explainability is not optional but mandatory. Emerging methods such as layer-wise relevance propagation (LRP), Grad-CAM, and attention-based transformers enable visualization of image regions driving model predictions. For example, saliency mapping applied to prostate cancer grading has demonstrated >85% concordance between AI-highlighted regions and pathologist-selected areas of diagnostic importance. Moving forward, the emphasis will be on regulatory-grade interpretability frameworks, wherein models provide both quantitative confidence scores and human-readable morphological rationales. Such systems could potentially reduce false positives by 20–30% in external validation studies, enhancing clinical trust and bridging the gap between AI inference and pathological reasoning.[34]

6.2. Federated learning and multi-institutional data sharing

Data scarcity and bias represent structural barriers to robust AI development. Conventional training datasets often lack ethnic, demographic, and technical diversity, leading to performance drops of up to 25% when models are externally validated. Federated learning (FL) offers a solution by training models on distributed datasets without direct data transfer. Recent studies, such as in breast cancer lymph node metastasis detection, have shown that FL-trained models achieved AUC scores of 0.93–0.95 across 7 independent cohorts, significantly outperforming single-center models (AUC ~0.85). In addition, FL preserves patient privacy, ensuring compliance with GDPR and HIPAA while enabling global-scale collaboration. Future directions include integrating differential privacy algorithms and secure multiparty computation, which will be critical for international AI consortia and regulatory approval.[35]

6.3. Integration of multi-omics with histopathological features

Cancer is inherently a multi-scale disease, with morphology, genomics, and transcriptomics reflecting interconnected layers of tumor biology. AI models are now beginning to decode these links. For instance, DL systems trained on H&E slides have successfully predicted IDH1 mutation status in gliomas (AUC ~0.91), EGFR alterations in lung adenocarcinoma (AUC ~0.88), and microsatellite instability in colorectal carcinoma (accuracy ~85–90%). The future lies in multimodal AI platforms that fuse histopathological features with high-dimensional omics (genomics, proteomics, metabolomics) and clinical metadata. Such integrative pipelines could enable patient-specific digital twins, predicting therapeutic response trajectories and resistance mechanisms. This would represent a paradigm shift from morphology-based classification to systems-level oncology, advancing personalized cancer care.[36]

6.4. Real-world deployment: AI as a pathologist's Co-Pilot

While fully autonomous diagnostic systems remain aspirational, current clinical trends support AI as a decision-support co-pilot. In this role, AI assists with case triage, region-of-interest highlighting, and quantitative biomarker assessment. For example, deployment of AI-assisted prostate biopsy screening has reduced routine slide review time by ~30–40% while maintaining >95% sensitivity for clinically significant cancer. Similarly, in breast pathology, AI-aided mitotic counting has demonstrated inter-observer variability reductions of 25–35%, ensuring reproducible grading. Beyond efficiency, AI integration also supports resource-limited environments, where pathologist shortages remain critical. Here, cloud-based AI triage systems can prioritize high-suspicion cases, thereby improving turnaround times for life-saving diagnoses.[37]

6.5. Prospects for fully automated vs. Hybrid human–AI systems

Two divergent but complementary futures can be envisioned:

Fully Automated Systems: Advances in digital pathology, robotic slide handling, and end-to-end AI pipelines may eventually yield autonomous diagnostic workflows. Proof-of-concept systems have already reported whole-slide classification accuracies exceeding 90% in select cancer types. However, barriers such as medico-legal accountability, explainability, and ethical acceptability currently preclude unsupervised automation.[38,39]

Hybrid Human–AI Systems: More immediately feasible is a symbiotic model in which AI standardizes repetitive tasks (e.g., quantification of Ki-67, PD-L1, HER2) while pathologists adjudicate complex, heterogeneous, or borderline lesions. Evidence suggests this hybrid model can simultaneously reduce diagnostic turnaround by 25–40% and improve accuracy by 10–15% compared to manual workflows alone. Such frameworks align with regulatory guidance and foster clinical trust, making them the most viable translational path in the near-to-midterm. The future of AI in histopathology will be defined by explainable, federated, multimodal, and hybrid systems that prioritize clinical accountability and translational scalability. By evolving beyond algorithmic accuracy toward interpretability, integration, and workflow augmentation, AI has the potential to transform oncological pathology from a subjective, human-limited practice into a standardized, data-rich, and precision-driven discipline.[21]

7. Conclusion

The integration of AI into histopathological oncology represents one of the most transformative developments in modern diagnostic medicine. Over the past decade, AI-driven platforms, particularly those leveraging deep learning architectures, have demonstrated remarkable capabilities in tumor detection, grading, prognostication, and prediction of molecular alterations directly from digitized whole-slide images. These advances underscore the potential of AI to overcome some of the long-standing limitations of conventional pathology, such as inter-observer variability, diagnostic delays, and challenges in quantifying subtle morphological features. By offering objective, reproducible, and high-throughput analysis, AI systems have already begun to redefine the diagnostic landscape, moving toward a future where precision oncology is anchored not only in molecular biology but also in computational pathology. Nevertheless, despite these encouraging developments, AI should be regarded as an augmentation tool rather than a replacement for human expertise. Pathologists remain indispensable, particularly in adjudicating ambiguous cases, contextualizing results within the broader clinical narrative, and ensuring accountability in patient care. The most pragmatic near-term vision is the hybrid human–AI model, where computational systems accelerate routine tasks and highlight diagnostically relevant regions, while expert pathologists provide oversight and interpretive depth. Looking forward, the roadmap for clinical translation requires prioritizing explainability, data standardization, federated learning frameworks, and robust regulatory validation. Future research must also emphasize the integration of multi-omics and real-world deployment strategies tailored to diverse clinical settings. Ultimately, the synergy of human expertise with AI’s computational power has the potential to establish a new gold standard in cancer diagnostics, advancing precision medicine and improving patient outcomes globally.

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9. Conflict of Interest

None.

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. https://doi.org/10.3322/caac.21834
2. Tseng LJ, Matsuyama A, MacDonald-Dickinson V. Histology: The Gold Standard for Diagnosis? *Can Vet J*. 2023;64(4):389–91.
3. Van den Bent MJ. Interobserver Variation of the Histopathological Diagnosis in Clinical Trials on Glioma: A Clinician's Perspective. *Acta Neuropathol*. 2010;120(3):297–304. https://doi.org/10.1007/s00401-010-0725-7
4. Masjoodi S, Anbardar MH, Shokripour M, Omidifar N. Whole Slide Imaging (WSI) in Pathology: Emerging Trends and Future Applications in Clinical Diagnostics, Medical Education, and Pathology. *Iran J Pathol*. 2025;20(3):257–65. https://doi.org/10.30699/ijp.2025.2044210.3367
5. Mohammed S, Malhotra N. Ethical and Regulatory Challenges in Machine Learning-Based Healthcare Systems: A Review of Implementation Barriers and Future Directions. BenchCouncil Trans. *Benchmarks Stand Eval*. 2025;5(1):6. https://doi.org/10.1016/j.tbench.2025.100215
6. Shafi S, Parwani AV. Artificial Intelligence in Diagnostic Pathology. *Diagn Pathol*. 2023;18(1):109. https://doi.org/10.1186/s13000-023-01375-z
7. Petríková D, Cimrák I. Survey of Recent Deep Neural Networks with Strong Annotated Supervision in Histopathology. *Computation*. 2023;11(4):81. https://doi.org/10.3390/computation11040081
8. Faa G, Castagnola M, Didaci L, Coghe F, Scartozzi M, Saba L, et al. The Quest for the Application of Artificial Intelligence to Whole Slide Imaging: Unique Prospective from New Advanced Tools. *Algorithms*. 2024;17(6):254. https://doi.org/10.3390/a17060254
9. Greeley C, Holder L, Nilsson EE. Scalable Deep Learning Artificial Intelligence Histopathology Slide Analysis and Validation. *Sci Rep*. 2024;14:26748. https://doi.org/10.1038/s41598-024-76807-x
10. Tiwari A, Ghose A, Hasanova M, Faria SS, Mohapatra S, Adeleke S, et al. The Current Landscape of Artificial Intelligence in Computational Histopathology for Cancer Diagnosis. *Discov Oncol*. 2025;16(1):438. https://doi.org/10.1007/s12672-025-02212-z
11. Afonso M, Bhawsar PMS, Saha M, Almeida JS, Oliveira AL. Multiple Instance Learning for WSI: A Comparative Analysis of Attention-Based Approaches. *J Pathol Inform*. 2024;15:100403. https://doi.org/10.1016/j.jpi.2024.100403
12. Manakitsa N, Maraslidis GS, Moysis L, Fragulis GF. A Review of Machine Learning and Deep Learning for Object Detection, Semantic Segmentation, and Human Action Recognition in Machine and Robotic Vision. *Technologies*. 2024;12(2):15. https://doi.org/10.3390/technologies12020015
13. Collins GS, Dhiman P, Ma J, Schlussel MM, Archer L, Van Calster B, et al. Evaluation of Clinical Prediction Models (Part 1): From Development to External Validation. *BMJ*. 2024;384:e074819. https://doi.org/10.1136/bmj-2023-074819
14. Whitney HM, Drukker K, Giger ML. Performance Metric Curve Analysis Framework to Assess Impact of the Decision Variable Threshold, Disease Prevalence, and Dataset Variability in Two-Class Classification. *J Med Imaging*. 2022;9(3):035502. https://doi.org/10.1117/1.JMI.9.3.035502
15. Wang J, Wang T, Han R, Shi D, Chen B. Artificial Intelligence in Cancer Pathology: Applications, Challenges, and Future Directions. *Cytojournal*. 2025;22:45. https://doi.org/10.25259/Cytojournal_272_2024
16. Yuan B, Hu Y, Liang Y, Zhu Y, Zhang L, Cai S, et al. Comparative Analysis of Convolutional Neural Networks and Transformer

Architectures for Breast Cancer Histopathological Image Classification. *Front Med*. 2025;12:1606336. https://doi.org/10.3389/fmed.2025.1606336
17. Singh NN, Tandon A, Jayasankar P. Strength, Weakness, Opportunities and Challenges (SWOC) Experience of Histopathology Image Analysis, Enhanced by Artificial Intelligence. *J Oral Biol Craniofac Res*. 2025;15(5):1057–63. https://doi.org/10.1016/j.jobcr.2025.07.013
18. Xie T, Huang A, Yan H, Ju X, Xiang L, Yuan J. Artificial Intelligence: Illuminating the Depths of the Tumor Microenvironment. *J Transl Med*. 2024;22(1):799. https://doi.org/10.1186/s12967-024-05609-6
19. 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. https://doi.org/10.1038/s44303-024-00020-8
20. Abdalhalim AZA, Ahmed SNN, Ezzelarab AMD, Mustafa M, Albasheer MGA, Ahmed REA, et al. Clinical Impact of Artificial Intelligence-Based Triage Systems in Emergency Departments: A Systematic Review. *Cureus.* 2025;17(6):e85667. https://doi.org/10.7759/cureus.85667
21. Saraf SA, Singh A, Teng WPK, Karakaya S, Logaswari M, Taghipour K, et al. Improving the Accuracy of Reporting Ki-67 IHC by Using an AI Tool. *Heliyon*. 2024;10(22):e40193. https://doi.org/10.1016/j.heliyon.2024.e40193
22. Ahn JS, Shin S, Yang SA, Park EK, Kim KH, Cho SI, et al. Artificial Intelligence in Breast Cancer Diagnosis and Personalized Medicine. *J Breast Cancer*. 2023;26(5):405–35. https://doi.org/10.4048/jbc.2023.26.e45
23. Bulten W, Kartasalo K, Chen PHC, 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. https://doi.org/10.1038/s41591-021-01620-2
24. Zehra T, Parwani A, Abdul-Ghafar J, Ahmad Z. A Suggested Way Forward for Adoption of AI-Enabled Digital Pathology in Low Resource Organizations in the Developing World. *Diagn Pathol*. 2023;18(1):68. https://doi.org/10.1186/s13000-023-01352-6
25. Zubair M, Owais M, Hassan T, et al. An Interpretable Framework for Gastric Cancer Classification Using Multi-Channel Attention Mechanisms and Transfer Learning Approach on Histopathology Images. *Sci Rep*. 2025;15(1):13087. https://doi.org/10.1038/s41598-025-97256-0
26. Innani S, Bell WR, Harmsen H, Nasrallah MP, Baheti B, Bakas S. Interpretable Artificial Intelligence Based Determination of Glioma IDH Mutation Status Directly from Histology Slides. *Neurooncol Adv*. 2025;7(1):vdaf140. https://doi.org/10.1093/noajnl/vdaf140
27. d'Amati A, Baldini GM, Difonzo T, Santoro A, Dellino M, Cazzato G, et al. Artificial Intelligence in Placental Pathology: New Diagnostic Imaging Tools in Evolution and in Perspective. *J Imaging*. 2025;11:110. https://doi.org/10.3390/jimaging11040110
28. Komura D, Ochi M, Ishikawa S. Machine Learning Methods for Histopathological Image Analysis: Updates in 2024. *Comput Struct Biotechnol J*. 2024;27:383–400. https://doi.org/10.1016/j.csbj.2024.12.033
29. Asif A, Rajpoot K, Graham S, Snead D, Minhas F, Rajpoot N. Unleashing the Potential of AI for Pathology: Challenges and Recommendations. *J Pathol*. 2023;260(5):564–77. https://doi.org/10.1002/path.6168
30. Cheng Z, Wu Y, Li Y, Cai L, Ihnaini B. A Comprehensive Review of Explainable Artificial Intelligence (XAI) in Computer Vision. *Sensors*. 2025;25(13):4166. https://doi.org/10.3390/s25134166
31. Akingbola A, Adegbesan A, Ojo O, Alao UH, Shagaya U. Ethical Challenges in the Integration of Artificial Intelligence in Palliative Care. *J Med Surg Public Health*. 2024;4:100158. https://doi.org/10.1016/j.glmedi.2024.100158
32. Bellahsen-Harrar Y, Lubrano M, Lépine C, Beaufrère A, Bocciarelli C, Brunet A, et al. Exploring the Risks of Over-Reliance on AI in Diagnostic Pathology: What Lessons Can Be Learned to Support the Training of Young Pathologists? *PLoS One*. 2025;20(8):e0323270. https://doi.org/10.1371/journal.pone.0323270
33. Vargas-Santiago M, León-Velasco DA, Maldonado-Sifuentes CE, Chanona-Hernandez L. A State-of-the-Art Review of Artificial Intelligence (AI) Applications in Healthcare: Advances in Diabetes, Cancer, Epidemiology, and Mortality Prediction. *Computers*. 2025;14:143. https://doi.org/10.3390/computers14040143
34. Gupta S, Dubey AK, Singh R, Kalra MK, Abraham A, Kumari V, et al. Four Transformer-Based Deep Learning Classifiers Embedded with an Attention U-Net-Based Lung Segmenter and Layer-Wise Relevance Propagation-Based Heatmaps for COVID-19 X-ray Scans. *Diagnostics*. 2024;14(14):1534. https://doi.org/10.3390/diagnostics14141534
35. Chen RJ, Wang JJ, Williamson DFK, Chen TY, Lipkova J, Lu MY, et al. Algorithmic Fairness in Artificial Intelligence for Medicine and Healthcare. *Nat Biomed Eng*. 2023;7(6):719–42. https://doi.org/10.1038/s41551-023-01056-8
36. Sartori F, Codicè F, Caranzano I, Rollo C, Birolo G, Fariselli P, et al. A Comprehensive Review of Deep Learning Applications with Multi-Omics Data in Cancer Research. *Genes*. 2025;16(6):648. https://doi.org/10.3390/genes16060648
37. Perumal MKK, Renuka RR, Subbiah SK, Natarajan PM. Artificial Intelligence-Driven Clinical Decision Support Systems for Early Detection and Precision Therapy in Oral Cancer: A Mini Review. *Front Oral Health*. 2025;6:1592428. https://doi.org/10.3389/froh.2025.1592428
38. Fatima G, Alhmadi H, Mahdi AA, Hadi N, Fedacko J, Magomedova A, et al. Transforming Diagnostics: A Comprehensive Review of Advances in Digital Pathology. *Cureus*. 2024;16(10):e71890. https://doi.org/10.7759/cureus.71890
39. Parvin N, Joo SW, Jung JH, Mandal TK. Multimodal AI in Biomedicine: Pioneering the Future of Biomaterials, Diagnostics, and Personalized Healthcare. *Nanomaterials*. 2025;15:895. https://doi.org/10.3390/nano15120895

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