

Review Article

Artificial Intelligence and Generative AI in Digital Pathology: Current Advancements, Clinical Applications, and Challenges in Global and Resource-Limited Settings


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Abstract

The emergence of artificial intelligence (AI) has been identified as a groundbreaking innovation in pathology, primarily facilitated by the progress achieved in digital pathology and whole-slide imaging. In recent years, generative forms of artificial intelligence, such as large language models and multimodal forms of AI, have further expanded the use of these tools to include research activities, documentation, and the integration of clinical information. The present review aims to present an overview of the current state of artificial intelligence in digital pathology, including the technological foundations, key diagnostic uses, and the potential role of generative forms of artificial intelligence. Recent systematic reviews suggest that AI algorithms demonstrate high accuracy for a number of histopathological activities. However, the implementation of these tools in routine pathology practice is limited by heterogeneity, a lack of external validation, and regulatory and ethical concerns. Special attention is devoted to the application of AI technologies in resource-constrained healthcare settings such as those in India, where infrastructure in digital pathology, training opportunities, and financial resources are still considered barriers.

Key words

Artificial Intelligence, Digital Pathology, Whole-slide imaging, Financial resources.

Introduction

Histopathological diagnosis has been based on microscopic examination of tissue sections after staining, where the patterns of morphology are examined to understand the underlying disease process. Although this method is considered the gold standard in diagnostic practice, the increasing number of cases and the level of diagnostic complexity have put immense pressure on the existing pathology infrastructure worldwide. The advent of digital pathology has revolutionized the existing diagnostic process in histopathology. The whole-slide imaging technique allows conventional glass slides to be converted into digital images that can be archived and remotely accessed for computational analysis [1, 2, 3]. The transition from optical microscopic techniques to digital image analysis has provided the basis for the development of computational pathology. Artificial intelligence is a group of computational techniques, including machine learning, deep learning, computer vision, and natural language processing, that enable computers to analyze patterns in large datasets and generate predictions [4, 5, 6].

Role of AI in Pathology

In pathology, these technologies have been found to possess promising capabilities in tumor detection, histological classification, grading of malignancies, and extraction of prognostic factors based on histopathological images. These deep learning-based approaches, in particular, have been found to achieve performance comparable to that of human pathologists in tasks such as the detection of metastases in lymph nodes and the classification of tumor types based on whole-slide histopathological images [7, 8, 9].

In addition to the progress being made in image-based AI, the emergence of generative artificial intelligence technologies has also opened up

possibilities for pathology workflows. These include the utilization of large language models and multimodal AI in tasks such as literature synthesis, research documentation, and the fusion of histopathological and clinical data [10, 11]. These technologies are intended to be employed as assistive technologies, not replacements, for human diagnostic capabilities. While the research outcomes are encouraging, the clinical utilization of AI technologies remains limited. The main challenges include differences in training data, lack of external validation, lack of interpretability in deep learning-based approaches, and regulatory ambiguity in medical AI technologies [12].

These challenges are especially important in a resource-limited healthcare system where digital pathology infrastructure and computational skills are still evolving [13]. In countries such as India, artificial intelligence may help improve pathology infrastructure, but for that, careful planning, infrastructure development, and training programs are necessary.

Digital Pathology Infrastructure and Workflow

Digital pathology is the technology infrastructure that enables artificial intelligence-based diagnostic tools. Traditional histopathology practice relies on microscopic examination of tissue sections on glass slides prepared from tissue sections fixed in formalin and embedded in paraffin. Whole slide imaging technology allows these glass slides to be scanned and transformed into a digital format for computational analysis [1].

The images captured by whole slide scanners have gigapixel resolution, allowing for visualization of cellular and tissue structures similar to that achieved by traditional microscopy. The digital pathology workflow

starts with conventional tissue processing and slide preparation, including tissue fixation, embedding in paraffin, microtomy, and histological staining [7]. Hematoxylin and eosin stain is the most common stain used for tissue sections, as it allows for visualization of tissue structures as well as cellular morphology. Once the slides are digitised, the images go through various preprocessing techniques to reduce the variability caused by different staining protocols or differences in technology. These preprocessing techniques may include stain normalisation, color correction, removing artifacts, and denoising [14]. The images of the slides are divided into smaller regions, called tiles or patches, for analysis by the computer. Deep learning techniques analyze these regions of the images to identify various morphological features, including tumor infiltration, necrosis, mitotic activity, and lymphocytic infiltration [15].

The use of computer systems for the analysis of digital images of pathology samples has given rise to a new branch of pathology, called computational pathology. This new branch of pathology combines digital pathology, artificial intelligence, and biomedical data science [9].

Digital pathology systems also enable telepathology, whereby a pathologist can access images and cases remotely and obtain a second opinion [16].

However, there is a significant barrier to the implementation of digital pathology systems. These systems require significant investments, and the infrastructural needs for a digital pathology system include a whole slide scanner, storage, and connectivity [17].

Artificial Intelligence Techniques Used in Pathology

Artificial intelligence in pathology includes a range of computer-based techniques for the analysis of complex histopathological images. The initial machine learning systems utilized

manually extracted features, including nuclear features, glandular features, and texture features. These features were then analyzed using statistical classifiers, including support vector machines and random forests [18]. These techniques were effective, but their capabilities were limited by the inability to automatically extract features.

The use of deep learning techniques has significantly improved the capabilities of machine learning systems for the analysis of images. Convolutional neural networks have shown significant capabilities for the analysis of histopathological images [4].

The use of deep learning systems has shown significant capabilities for various diagnostic tasks, including tumor detection, tumor grading, lymph node metastasis, and histological classification. CNN systems for the analysis of WSI images have shown significant capabilities for the detection of metastatic breast carcinoma in lymph node sections [7]. More interest has also been paid to explainable techniques in artificial intelligence. Techniques like attention map and feature visualisation are intended to enhance the interpretability of deep learning technology and thus build confidence in decision-making processes. **Table - 1** summarizes major artificial intelligence techniques used in digital pathology.

Clinical Applications of Artificial Intelligence in Diagnostic Pathology

Artificial intelligence has proven to be effective in several diagnostic procedures in histopathology. It can evaluate digitized WSIs to assist pathologists in detecting malignancies, classifying tumor types, and determining tumor micro-environment features [13].

One of the most commonly evaluated applications of AI in histopathology has been tumor detection in lymph nodes. Deep learning algorithms have proven to be very accurate in detecting micrometastases and isolated tumor

cells. The CAMELYON challenge has demonstrated the capability of convolutional neural networks to detect breast cancer metastases in lymph nodes with comparable diagnostic performance to expert pathologists [7].

Table – 1: Major Artificial Intelligence Techniques Used in Digital Pathology.

Technique	Principle	Applications in Pathology
Machine learning [18]	Uses predefined image features with statistical classifiers	Early tumour classification and pattern recognition
Deep learning (CNNs) [4, 15]	Learns hierarchical image features directly from image data	Tumour detection, grading, and metastasis detection
Transformer models [10]	Captures contextual relationships across image regions	Complex pattern recognition
Generative AI [10, 12]	Produces synthetic data or text outputs	Dataset augmentation, literature synthesis

Table – 2: Clinical Applications of Artificial Intelligence in Histopathology.

Pathology Area	AI Method	Clinical Benefit
Breast cancer lymph node metastasis	Deep learning	Faster slide screening
Lung, breast and colorectal tumours	Deep learning	Diagnostic support
Immuno-oncology biomarkers	Image analysis algorithms	Prognostic insights
Microsatellite instability and mutations	Deep learning	Early molecular guidance

AI has also been used to classify tissues histologically and grade tumors. Deep learning algorithms can classify tumor types depending on tissue morphology in tissues from the lung, breast, and colon [8]. Another application of AI in histopathology has been to evaluate tumor micro-environment features. AI algorithms can quantify tumor-infiltrating lymphocytes, tumor stroma, and vasculature in tissue sections [9]. In addition, deep learning algorithms have proven to have the potential to predict molecular changes in tumor tissues directly from H&E-stained tissue sections, including microsatellite instability and certain mutations in tumor suppressor genes [19]. **Table - 2** summarizes clinical applications of artificial intelligence in histopathology.

Generative Artificial Intelligence in Pathology

In addition, the development of generative artificial intelligence has increased the range of AI applications in pathology beyond image classification. Generative artificial intelligence

can generate text, synthesize information, and produce synthetic images. Large language models are gaining popularity due to their ability to assist in summarizing medical literature, assist with research writing, and aid in educational activities [20]. Surveys conducted among pathology professionals revealed that AI applications are currently utilized to assist with research activities [11]. Generative adversarial networks and diffusion models can generate synthetic images that mimic actual tissue sections [21]. The images can be utilized to improve the robustness of machine learning models. Multimodal AI systems are another new trend in AI applications in pathology. In multimodal AI systems, histopathological images are combined with clinical records or genomic information to produce diagnostic results [22].

In spite of the benefits offered by generative AI systems, it has to be noted that these systems can sometimes generate false or fabricated information.

Challenges and Limitations of Artificial Intelligence in Pathology

While the promise of these technologies is high, there are still several challenges that need to be overcome in their clinical application. One of the limitations of current research in the application of AI technology is that the data available for training is heterogeneous in nature. Often, data is available in a controlled environment, and there are chances that the data might not be representative in real-world scenarios [12]. In addition, the studies conducted so far are limited in nature and need to be validated in real-world scenarios. Another challenge that needs to be overcome is ethical in nature. Issues related to bias, data privacy, and accountability need to be taken care of before the technology is deployed in real-world scenarios [11]. In countries like India, where resources are limited, the lack of digital pathology infrastructure and training opportunities are limitations in the application of technology [14].

Role of the Pathologist in AI-Assisted Diagnostics

The role of artificial intelligence should be seen as a supportive role rather than that of a standalone diagnostic tool. In the context of histopathological examination, the role of clinical judgment, morphological examination, and contextual judgment is important. Thus, the role of AI tools may be seen as supportive, where the pathologist may use the tools as a means of prioritizing the examination, highlighting suspicious areas, and carrying out quantitative analysis of the histological features. In this context, the ideal role is that of augmented intelligence, where the role of computers is to bring efficiency and enhanced capability, while the role of the pathologist is to bring accuracy, accountability, and appropriate clinical judgment.

Future Directions and Conclusion

The role of artificial intelligence will be critical in the future of digital pathology. Future research

will need large multi-institutional datasets, validation frameworks, and reporting guidelines [23]. Multimodal artificial intelligence will be an area for future research, which will include the integration of histopathology images with other data such as clinical and genomic information [22]. For countries with limited resources, the development of infrastructure and educational programs will be a future need to ensure the safe implementation of artificial intelligence [14].

Therefore, artificial intelligence should be considered an auxiliary tool to improve the efficiency of diagnosis rather than a replacement for human expertise. The collaboration between clinicians, data scientists, engineers, and policymakers will be critical to ensure the safe integration of artificial intelligence.

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