Review Article

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Intelligence meets morphology: The rise of artificial intelligence in modern pathology

Mansi Singal, Sonia Gon, Margareth Khuraijam

Department of Pathology, ESI-PGIMSR Medical College, Kolkata, West Bengal, India

Address for correspondence: Dr. Mansi Singal, Junior Resident, Department of Pathology, ESI-PGIMSR Medical College, Joka, Kolkata, West Bengal, India. E-mail: mansi.singal16@gmail.com

Abstract

Pathology is an inherently complex field relying heavily on subjective microscopic examination, leading to variability and inefficiency. Digital Pathology and the advent of Artificial Intelligence (AI) offer promising solutions to automate and standardize diagnostic workflows along with better tissue analysis by improving accuracy, reproducibility, and speed while supporting pathologists. In this review, all key advances have been demonstrated – including cancer detection, grading, and prognostication, highlighted by benchmark studies and challenges. Despite challenges such as data diversity, interpretability, and clinical validation, AI's integration with multiomics data presents a transformative opportunity for personalized and precision pathology. This review overall summarises current AI capabilities, discusses practical considerations for clinical implementation, and outlines future directions, emphasizing interdisciplinary collaboration to realize AI's full potential in advancing pathology practice.

Keywords: Artificial intelligence, Convolutional neural network, Deep learning, Digital pathology, Generative adversarial network, Graph neural network, Machine learning

Introduction

Pathology is a field where most tasks are non-binary and context-dependent. Most traditional diagnostic methods of tissue analysis - histopathology, immunohistochemistry, and cytopathology - rely heavily on a highly subjective and time-consuming exercise of microscopic slide examination. The comprehensive nature of these subfields, which depends on inter-observer judgments and knowledge, along with the need for the use of manual techniques in tissue preparation involving intricate and independent steps,[1] makes them slow runners in making progress toward overcoming their subjective variabilities through automation. This change has been openly embraced by other subfields, such as clinical chemistry, laboratory medicine, and hematopathology. Implementation of an automated workflow system can help in many areas that pose a roadblock to overall performance efficiency, and the advent of Digital Pathology (DP) – particularly through Whole Slide Imaging (WSI) – was a significant step forward[1,2] in striving for such transformation into a more automated and objective science.

The foundation for digital imaging in pathology was laid decades ago when researchers such as Prewitt and Mendelsohn[3,4] developed early techniques to convert blood smear visuals into matrices of optical density values that preserved the spatial information such that rudimentary cell classification could be done. The emergence of Artificial Intelligence (AI) has been a further step ahead in DP,[5] and it has managed to largely address the problems of variability and inefficiencies

associated with subjective cumbersome tasks, spanning from low-level ones such as object recognition and classification to high-level ones involving image analysis[6] that helps in predicting the diagnostic and prognostic aspects of disease, including assays to evaluate disease severity and outcome.[4]

AI-based approaches are based on image analysis, segmentation, detection, and diagnosis. Within AI, two main algorithms have become essential. machine learning (ML) algorithms that learn patterns from input data to make informed output predictions, and deep learning (DL), which is an advanced branch that uses a multilayered artificial neural networks, mimicking the neural framework of human brain,[7] to autonomously generate and refine features from complex datasets like images. DL has enhanced diagnostic and treatment decision-making processes, and with the synergistic rising power of computational resources, it has demonstrated the ability to match, and at times complement, the diagnostic accuracy of human experts. A pioneering study by Mukhopadhyay[8] has shown that digital diagnosis using WSIs is non-inferior to traditional microscopy, and subsequently, several articles have critically examined the advantages of DL in this domain, including those by Srinidhi *et al*.,[9] Tran *et al*.,[10] She Y *et al*. (2020),[11] focusing specifically on cancer diagnosis.

Another attempt to drive innovation and identify talents has been through the first major challenge, called CAMELYON16, aimed to develop AI tools for detecting breast cancer metastases in H&E-stained lymph node slides.[1,6] It also compared the accuracy of algorithms with that of medical students and expert pathologists. The dataset created for CAMELYON16 has since been widely used in research and inspired future challenges.[12,13]

In histopathology, AI tools offer a way to extract numerous subtle, sub-visual features from standard H&E-stained tissue sections.[4] While challenges such as tumor heterogeneity and sampling bias remain[14,15] these automated approaches allow for more reproducible, multi-dimensional interpretations of tissue architecture. Ultimately, integrating AI with radiological, proteomic, and genomic data has the potential to provide a more functionally relevant diagnosis.[16]

With this review, we aim to provide a comprehensive overview of how AI is transforming the field of pathology by evaluating the current capabilities of AI across key pathology tasks, such as cancer detection and grading, while also addressing the challenges and practical considerations for clinical integration. By synthesizing recent advances and benchmark studies, the article seeks to inform pathologists, clinicians, and researchers about the evolving role of AI in pathology and offer insights into future directions for implementation and innovation.

Technical Foundations of AI in Pathology

Computer-aided diagnosis (CAD)

Before advanced ML and DL models became popular in DP, CAD systems were used for image analysis in conjunction with ML, acting as second opinions to help reduce workload, errors, and costs.[17] The principle on which these CAD systems worked often mimicked how doctors look at tissue, especially the shape and features of cell nuclei, to detect cancer. Primitive use of CADs can be evidenced in the context of breast carcinoma studies by Brook *et al*.,[18] Zhang,[19] Kowal *et al*.[20] and Filipczuk *et al*.[21]

ML

The foundational algorithm of AI involves ML models that can make predictions on the basis of specific characteristics from images. In a basic sense, ML is a computer agent that learns from its environment to improve performance.[22] On a functional level, ML encloses either of the two types of domain features – domain-inspired or domain-agnostic;[4] both encompassing an umbrella term called "feature engineering."[7,23-25] Domain-

inspired features need reliance on the expertise of pathologists or oncologists to design features tailored to a specific disease or tissue type, like mitotic figure count in breast cancer, which is a subjective task done by pathologists and cannot be replicated broadly for other diseases.[7] Another example of a domain-inspired feature is assessing the angularity of glands in prostate cancer, where the measurement of how disorganized or chaotic the gland directions are in tissue determines the aggressiveness of the cancer. This has been the subject of a study by Lee *et al*.[26]

On the other end are domain-agnostic features that do not rely on medical expertise and can be applied across different tissues and diseases, including but not limited to texture patterns, nuclear shape, and size, or the spatial arrangement of cells using graph-based approaches.[4] Domain-agnostic features allow for the measurement and analysis of the structure and spatial organization of individual tissue components – such as lymphocytes or glands – as well as the relationships between different types of tissue-specific elements. A classic example is the use of texture features in the grading of prostate cancer (Gleason's grading)[26,27] which distinguishes between low and high-grade tumors. Oropharyngeal tumors[28] are also such tumors where both domain-specific and domain-agnostic handcrafted approaches have been useful in diagnosing, grading, and predicting treatment outcomes. Similarly, both play complementary roles in distinguishing low-grade gliomas from high-grade gliomas in histopathology images, as in a study by Elazab *et al*.[29,30]

The use of graph-based ML models has been found to be significant in assessing prognosis in several cancers.[31] This has been done through analysis of spatial tissue architecture. A convolutional neural network (CNN), explained in detail in subsequent sections, was used by Saltz *et al*.,[32] with pathologist feedback, to detect spatial patterns of tumor-infiltrating lymphocytes (TILs) across 13 different cancer types on slides taken from The Cancer Genome Atlas, and it was noted that they showed an overall strong prognostic value.[4,32] It was also found that in early-stage non-small cell lung cancer (NSCLC), the spatial relationships between TILs and cancer cells (captured through graph-based modeling) predicted recurrence in a much better way as compared to TIL density alone.[33] Another similar study was by Yuan[34] which analyzed TIL distributions in triple-negative breast cancer and they found that the ratio of intratumoral lymphocytes to cancer cells is linked to survival and cytotoxic T lymphocyte protein 4 expression[4] This was later further extended to estrogen receptor (ER)-positive breast cancers as well, where they found similar associations with a late recurrence.[35] Beyond tumor cells, recent work has explored the prognostic role of stromal features also, with a study by Beck *et al*.[36] analyzing over 6000 features from epithelial and stromal regions in breast cancer WSIs and finding that stromal features have stronger associations with overall survival ($P = 0.004$) than epithelial ones ($P = 0.02$).[4,36] Another study by Ali *et al*. has found that combining nuclear features from both stromal and epithelial compartments improves predictions for an human papillomavirus (HPV)-positive oropharyngeal cancer progression. Another study by Ali *et al*. has found that combining nuclear features from both stromal and epithelial compartments improve predictions for an HPV-positive oropharyngeal cancer progression.[37]

In the context of diagnostic importance, there are many examples of studies where ML has used its image-based features to differentiate between malignant and benign tumors. One such example is a study by Lu *et al*.[28] where nuclear shape and texture diversity were used to predict disease-free survival in an oral cavity squamous cell carcinoma. Another study by Whitney *et al*.[38] showed that nuclear features could differentiate ER-positive breast cancer patients with short-term (<10 years) survival and long-term survival (>10 years), which predicted the recurrence risk using Oncotype DX scores. In another study by Osareh and Shadgar,[39] an ML model was used, with ten cellular features identified by an expert pathologist to classify breast tumors from fine-needle aspiration biopsy images.

In the area of disease management, ML has gained traction for identifying which patients may benefit from specific treatments. Wang *et al*.[40] used nuclear and perinuclear features to stratify early-stage NSCLC patients who had surgery into high- and low-risk groups for recurrence, helping to identify those who might benefit from adjuvant chemotherapy. In addition, they showed that the spatial arrangement of nuclei and TILs could predict response to anti-PD-1 therapy (nivolumab) in late-stage NSCLC patients.[40-42]

Taxonomy of ML

A way to better understand the role of ML in our daily life is by categorizing it into 4 types, as also mentioned in a 2022 study on the same. These include supervised, unsupervised, and weakly supervised learning (WSL), and reinforcement learning. The best among these is supervised learning[43] which requires labeled data where each input has a corresponding output and is mainly used for tasks such as classification and regression. The exercise of labeling data, however, is an especially time-consuming and expensive task in addition to being prone to human error. A contrasting method to this is unsupervised learning, which works on analysis without any labels and instead uncovers patterns through clustering, dimensionality reduction, association, and density estimation association.[44] There is less human input needed, so it is more intensive and less accurate.[45]

Along the spectrum of both these is WSL,[46] which addresses the weaknesses of both and is more commonly used for medical image analysis.[43] The labels used in this method are limited and not as precise as those in the supervised learning method. An example quoted in a study by Qu *et al*. is of lung cancer scans using incomplete supervision where only a few data points are labeled, like diagnosing an MRI image with the label "lung cancer" without being able to identify the exact tumor details. Often, the labels can be wrong due to annotator fatigue or inexperience, which accounts for a major limitation of this method.

An important innovation in WSL is Multiple Instance Learning (MIL), which treats an entire WSI as a "bag" of smaller patches, each inheriting the overall slide label. This approach was introduced by Dietterich *et al*.[47] in 1997, and extended to medical imaging by Quellec.[48] in 2017. It allows models to learn from coarse, slide-level annotations without requiring pixel labeling, and we can see 3 types of detections – global detection, local detection, and false-positive reduction. Several reviews provide further insights into these MIL types.[49,50]

Reinforcement learning involves agents interacting with environments and is useful in games or simulations, but the real-world use is limited due to complexity and safety concerns.[43] Several studies have explored WSL in medical imaging. like Rony *et al*.[51] studied WSL for histology image classification and localization, Qu *et al*. proposed a taxonomy of WSL methods (instance-based, bagbased, hybrid), though not comprehensive, Hassan *et al*.[52] focused on WSL with transfer learning and data augmentation for COVID-19 computed tomography scans and Zhou.[46] provided a broad overview but lacked more detail on medical imaging. Despite increasing interest in WSL since 2015, very few comprehensive reviews exist to address gaps in past research and highlight the need for precise, efficient ML solutions in healthcare.

DL

A subset of ML is another popular emerging field in DP called DL[53] which can automatically learn patterns from raw image data without the need for manually engineered features.

Unlike traditional ML approaches, DL models are trained on labeled images (e.g., benign vs. malignant tumors), and they identify the most useful image features on their own to distinguish between many categories. This has made the process not only highly accurate but also easier to implement as compared to hand-crafted feature-based methods.[4] The only downside so far seems to be a need for more data and computing power by DL models.

A cornerstone approach in DL analysis is through CNNs, which have shown substantial success in capturing image-level features.[17,53-55] CNNs learn features automatically and directly from the images, and there is no need for manual feature selection as seen in ML. Their ability to detect important features from input images makes them overall less biased by the dataset and enables them to work well across a wide range of tasks. There are many examples of studies exploring the utility of CNNs; one has been by Araújo *et al*.[17] and Esteva *et al*.,[56] where differentiation of benign nevi and malignant melanoma was done using this approach, and another by Tschandl *et al*.,[57] where CNNs ability to be as accurate as humans was explored by classifying pigmented skin lesions using digital dermatoscopic images.

The working principle of CNN involves learning and extracting parts from images using certain filters that exist in the form of multiple convolutional sheet networks. These sheets are independently layered as building blocks between the input and output layers, and they are not connected to each other.[4] Since the neuronal network in these sheets is not connected to the previous layer, small portions of the image can be efficiently focused on. This speeds up processing, and the pooling layers also reduce the size of the data while retaining important information. In the MIDOG challenge,[58] CNNs were used to address mitosis detection across diverse domains. Spanhol *et al*.[59] used it on small image patches (32 × 32, 64 × 64), which delivered an overall good accuracy but with a downside of weaker output at high magnification. Larger patches (101 × 101) were used in a subsequent study by Ciresan *et al*.,[60] detecting mitosis accurately. This significantly paved the way for CNNs to excel in mitosis detection. In addition to identifying key tissue features like mitotic figures, CNNs have also been used detecting and measuring cells (such as lymphocytes or neutrophils), identifying nuclei, stroma, or glands, and highlighting important areas such as tumors or surrounding tissue. They have played a key role in automating Gleason grading and prostate cancer diagnosis.[61] In addition, CNN-based models have been employed for feature extraction to classify brain tumor grades and for accurate mitosis detection in breast cancer.[62] In histology, CNNs have enabled effective nuclei segmentation, even under weakly supervised training conditions,[63] demonstrating their adaptability and robustness across tasks. One system called DeepFocus by Brixel *et al*.[64] uses CNNs to find and remove blurry or out-of-focus areas in WSIs with an accuracy of 93.2% (±9.6%).[4]

Graph neural networks (GNNs) are gaining prominence as a powerful extension of DL, particularly suited to domains where data is relational and irregularly structured. Many forms of medical data are better modeled as graphs, where relationships between entities are crucial. In addition to using ML to classify immune cells and tumor cells, a graph-based description of TILs and neoplastic cells pattern can be used to describe spatial interactions between both (SpaTILs score) and TIL clusters density patterns. These scores can be used to predict recurrence and adjuvant therapy success (as studied by Azarianpour *et al*.).[65] A study in 2020 used a similar workflow to first classify between stromal, immune and neoplastic cells in melanomas and then describe the spatial arrangement of those cells from a graph-based approach.[31] However, while GNNs have shown promise, their use in the medical field remains relatively under-explored compared to traditional DL methods, and research on GNN interpretability is still immature, with few clinical applications so far.

Generative AI approaches

Generative adversarial networks (GANs) are another type of DL model that can create, in a crude sense, a realistic-looking fake image by learning from a real one.[66,67] In a technical sense, GAN's working principle is based on 2 competing neural networks, where one network (generator) produces synthetic (fake) data from the exemplars fed to the network, while the second one (discriminator) assesses the concordance between the original and generated (fake) data. The goal is to reduce the classification error of the second network in

a way that produces the closest possible output to the original image. GANs are used in histology for data augmentation, i.e., making more realistic tissue images to train other models and helping researchers when real medical images are limited. An upgrade to this is a Conditional GAN (cGAN), which adds extra information (like labels or categories) to guide the image generation.[68] For example, cGAN generates "lung cancer" tissue images exclusively instead of random ones.[69] This makes the output overall more controlled and useful for specific tasks.

Figure 1 gives a conceptual overview illustrating the transition from early rule-based CAD systems to advanced DL frameworks. It highlights how AI models have progressed from manual, feature-based analysis (domain-inspired and domain-agnostic) to automatic features such as CNNs, spatial graph modeling (GNNs), and synthetic data generation (GANs/cGANs) for robust tissue interpretation.

Clinical Applications and Impact

Cancer detection and diagnosis

The most common applications of AI have been for malignancies, with its wide role in detection, grading, prognosis prediction, therapeutic target identification, and molecular profiling.[4] Although limited, among its noncancer diagnostic applications, one is its use in the classification of kidney biopsies.[70,71] There have been few studies that show enhanced sensitivity of the AI system as compared to human analysis, with one study showing 99% accuracy of AI in detecting breast cancer metastases in lymph nodes, compared to 81% for pathologists.[6] Similar findings have been further extended to other cancers, including colon cancer, head and neck cancer, and melanoma, paving the way for reduced diagnostic errors and improved classification accuracy, which is crucial for choosing the right

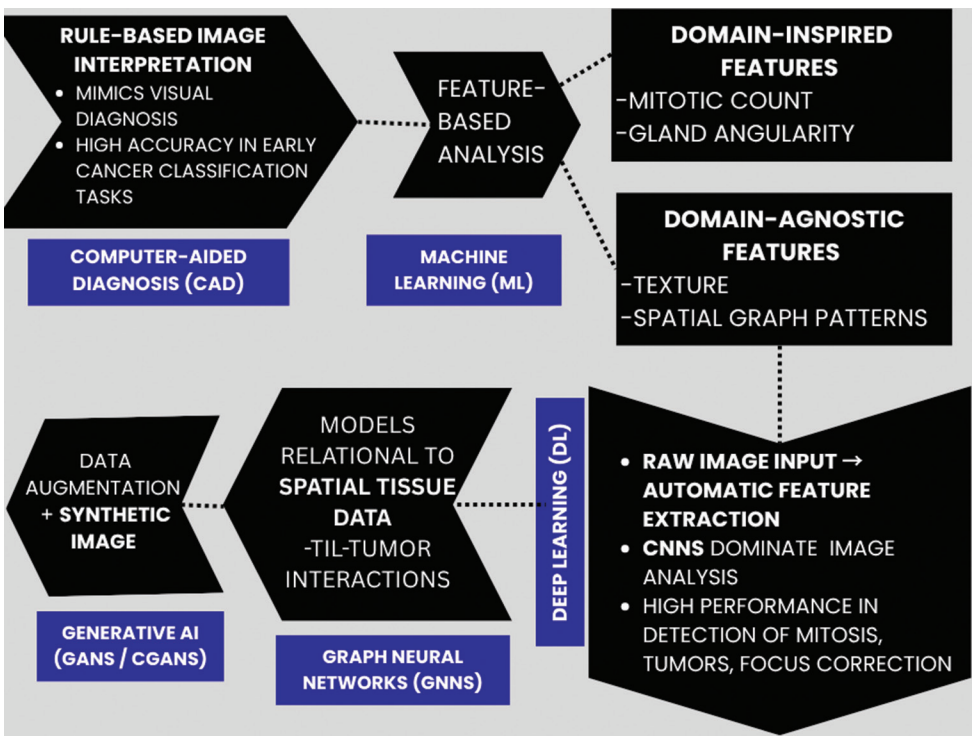

Figure 1: Evolution of computational pathology approaches, showing the transition from rule-based CAD systems to deep learning frameworks (CNNs, GNNs, GANs/cGANs) for advanced tissue interpretation.

treatment. Several cytopathology applications of AI have also demonstrated relatively high algorithmic sensitivity. In cervical intraepithelial lesion screening, sensitivities range from 85.7% to 94.7%.[72] Similarly, lung cancer detection using AI has shown both high sensitivity and specificity of 95.9% and 98.2%, respectively.[73] Furthermore, even for urine cytology, the sensitivity and specificity achieved by AI models are 80.9% and 61.8%, respectively,[74] when benchmarked against histopathological findings, which shows a promising applicability of the AI models for clinical pathology and cytopathology.

Tumor grading with AI

ML has become a vital tool in histological image classification, evolving from traditional pipelines to more advanced DL approaches. As discussed, the process begins with a dataset of microscopic images labeled by experts as tumoral or non-tumoral, and classical image analysis methods are then used to extract features such as color and texture, which are fed into ML classifiers for training. Further, DL has transformed this workflow using neural networks[4] – composed of multiple layers of perceptrons trained through gradient descent and backpropagation – to automatically learn both features and decision rules. While this improves performance, it also introduces challenges in interpretability, which is especially critical in clinical applications. However, these tools have shown significant promise in histopathology, specifically for tumor grading across various cancer types by reducing observer variability.[75] In prostate cancer, Gleason grading is a critical prognostic tool, but it is traditionally affected by inter-observer differences among pathologists, and many DL models have demonstrated pathologist-level performance in this domain.[26,61,76] Similarly, studies by Arvaniti *et al*.,[77] Nagpal *et al*.,[78] and Bulten *et al*. (2020)[79] also reported high accuracy of DL-based systems in grading tissue microarrays and biopsies.

In breast cancer, the Nottingham grading system presents unique challenges, mainly in mitosis detection, which was emphasized in the MITOS-ATYPIA-14.[80] Similarly, in colorectal adenocarcinomas, glandular architecture plays a key role in tumor grading, so a study by Sirinukunwattana *et al*.[81] tackled gland segmentation challenges, while Awan *et al*. employed gland shape features in ML models to predict tumor grade.[82] Across all these domains, AI has not only automated and standardized grading, but it also supports more reproducible and scalable diagnostic workflows.

Predicting genetic alterations

DL is increasingly being used to predict genetic alterations directly from histological slides, providing cost-effective and rapid alternatives to traditional molecular testing. One key application has been in detecting microsatellite instability (MSI), which arises from defects in DNA mismatch repair genes and is especially prevalent in gastrointestinal cancers. MSI has major therapeutic significance, as MSI-high tumors are highly responsive to immunotherapy. Several studies have shown that DL can predict MSI status from histopathology slides, as summarized by Klein *et al*.[83] Echle *et al*. further validated this approach by training DL models on 8836 WSIs of colorectal cancer (CRC), underscoring its clinical utility.[84] Another emerging use of AI is in detecting virus-associated cancers, such as those linked to HPV and Epstein–Barr virus (EBV). Jouhi *et al*.[85] and Klein *et al*.[83] highlighted the importance of detecting these oncogenic viruses, with EBV-positive gastric cancers showing notable response to PD-1 inhibitors. Kather *et al*.[86] demonstrated that DL models can identify HPV in head-and-neck cancers and EBV in gastric cancers using morphological features alone. Beyond specific mutations or viral associations, A study in 2020 showed that DL models could predict broader genomic events – such as whole genome duplication, aneuploidy, and transcriptomic profiles – across 28 cancer types using 17,396 WSIs.[83] These advancements signal a shift toward integrating AI-based histopathology with genomics for precision oncology.

Prognosis prediction

DL approaches have begun to surpass the traditional methods of prognostic prediction in oncology, which relied on statistical models such as Cox regression (that estimate survival based on clinical and pathological features), by leveraging rich morphological data from histological images. For instance, Wang.[24] developed a shape-based model using features extracted from lung adenocarcinoma images, while Tabibu *et al*.[87] used nuclei and tumor morphology to predict outcomes in renal cell carcinoma. Kather *et al*.[88] introduced a novel "deep stroma score" derived from CRC WSIs, correlating stromal patterns with prognosis.

A more advanced method, Survival CNNs (SCNNs), enables direct prediction of patient risk from histological tiles. Zhu *et al*.[89] showed that SCNNs outperformed traditional Cox models in lung cancer prognosis, whereas Mobadersany *et al*. and Courtiol *et al*. applied this to glioma and mesothelioma,[90,91] discovering both known and novel prognostic markers. In hepatocellular carcinoma, a series of studies by Calderaro *et al*. highlighted DL's ability to detect morphological features linked to survival outcomes.[92] Finally, Skrede *et al*.[93] demonstrated that an ensemble DL model could outperform conventional prognostic markers in CRC, showcasing the growing potential of AI to revolutionize risk stratification and treatment planning.

Tumor immune microenvironment (TILs)

The tumor immune microenvironment, particularly the presence and composition of TILs, plays a critical role in determining cancer prognosis and response to immunotherapy. Specific immune cell types carry prognostic significance: CD8+ cytotoxic T cells are generally associated with better outcomes,[83] whereas regulatory T cells (Tregs) marked by FoxP3 expression often indicate a poorer prognosis.[94] To standardize TIL evaluation, several quantitative methods have been developed. Guidelines for assessing immune infiltrates on H&E-stained slides were proposed.[95,96] Notably, there are studies that introduced the immuscore, based on CD3 and CD8 T-cell densities, which was validated in over 2500 CRC patients across 13 countries.[83] Other studies employed spatial density profiling of lymphocytes to refine immune landscape evaluation. However, manual interpretation and variability in immunohistochemical (IHC) staining, especially for programmed death-ligand 1 (PD-L1), pose challenges, underlining the need for automated, AI-powered methods for reproducible and scalable immune profiling in clinical pathology.[97]

Predictive biomarkers and precision oncology

CNNs have been applied to automate the analysis of IHC labeling, such as human epidermal growth factor receptor 2 (HER2), a critical biomarker in breast cancer diagnosis, as also demonstrated in a study by Qaiser *et al*., in 2018, called the HER2 challenge.[98] Similar approaches have been used to detect immune cells labeled for CD3, CD8, CD20, CD3, CD8, CD45, and for PD-L1 scoring. These methods enhance detection accuracy by reducing labeling variability within and across slides.[83] In addition, DL and ML can classify tissue subtypes to automatically define regions of interest, enabling subsequent quantification of labeled lymphocyte subtypes using classical image analysis (Reichling *et al*., 2020).[99]

Cytopathology and subspecialty applications

AI in cytopathology offers multiple applications and benefits. It assists in cell classification, detecting abnormalities, and predicting disease progression using annotated datasets. CAD systems, as discussed before, improve accuracy in certain cancers like urothelial carcinoma assessment. ML tools support seamless integration with ultrasound and fine-needle aspiration cytology. There has been a significant advancement in the field of cytopathology, with AI assisting in the early detection of thyroid cancers. It has shown potential as a diagnostic aid with studies such as

one by Tessler and Thomas that highlight AI's effectiveness in evaluating thyroid malignancy.[100] Beyond thyroid applications, AI is also being explored in specialized cytopathology areas such as fungal cytology, where AI aids in identifying oral dysplasia using CD44-SNA1 markers.[101] Moreover, AI-driven survival prediction models have been applied to various non-gynecologic cancers. In urinary tract and thyroid cytopathology, AI has demonstrated improvements in diagnostic accuracy and risk stratification, indicating its growing role in precision medicine.

Integration with Clinical Workflows, Challenges, and Risk Mitigation

While AI has revolutionized pathology by improving diagnostic accuracy and efficiency, it also introduces significant risks. These include algorithmic bias due to training on non-representative datasets, reduced transparency in decision-making (particularly with DL's "black box" nature),[102] and potential over-reliance on automated systems. Moreover, without rigorous validation across diverse clinical settings, AI models risk producing misleading results that could adversely impact patient care. Data privacy and security concerns also loom large, especially when handling sensitive patient information. Critically, the quality and diversity of the image datasets used to train these models play a central role in determining their generalizability and reliability in clinical practice. To address these risks, robust mitigation strategies must be implemented. These include using diverse, high-quality datasets for model training and validation, incorporating explainable AI approaches to enhance model transparency, and fostering a collaborative workflow where AI complements (rather than replaces) pathologist expertise. The need for continuous model updating (to incorporate new data and avoid performance degradation over time) and the importance of interdisciplinary training (to help pathologists and data scientists work seamlessly together) are extremely key to achieving this.

Future Directions

Emerging trend of spatial transcriptomics

Spatial transcriptomics is a groundbreaking method that maps gene activity directly onto their physical locations within intact tissue, letting researchers see not just which genes are active, but where they are while keeping tissue structure intact.[103] AI and DL, especially tools like CNNs, have improved how we analyze images of tissues. Since spatial transcriptomics include both gene expression and images, combining the two can give a fuller picture of tissue biology. However, it is difficult to merge these high-dimensional data types due to different expertise and challenges in interpreting image features. To address this, a structured approach is needed, which can be achieved by either of these 2 strategies, as explored in a review article by Chelebian *et al*. Translation, which uses image features to predict gene expression (faster and cheaper), or integration which combines both types of data for deeper insight.[104]

AI chatbots for report interpretation

A recent 2024 study by Steimetz *et al*. explored the use of generative AI chatbots to simplify pathology reports for patients.[105] Inspired by an earlier work showing that chatbots can offer empathetic responses, their study highlighted the potential to support rather than replace physicians by making complex medical information more understandable. This revolved around the idea of helping patients with low health literacy, ultimately improving engagement in their care.

Chatbots could also streamline clinical workflows by automatically categorizing reports (e.g., benign, premalignant, malignant), allowing faster triage and potentially releasing benign results directly to patients without delay. Fine-tuning models may improve reliability, but until then, chatbot outputs should be reviewed by clinicians.

Conclusions

AI has emerged as a powerful tool in modern pathology, offering solutions to longstanding challenges in diagnostic accuracy, reproducibility, and efficiency. While these technological advances have already demonstrated significant clinical impact–particularly in cancer detection, prognosis, and molecular characterization–there remain important hurdles to widespread implementation, including issues of data diversity, model interpretability, and clinical validation.

As AI continues to evolve, fostering interdisciplinary collaborations between pathologists, data scientists, and regulatory bodies will be key to realizing its full potential in delivering precision, equity, and personalized care to patients.

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