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Article

The Role of Artificial Intelligence in Histopathological Image Analysis

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Abstract: Histopathology is the science of diagnosing diseases based on tissue morphology, enabling us to understand what kind of disease (as well as prognosis) a patient has. Artificial intelligence (AI), specifically machine learning and deep learning methods, have reached into the field of pathology to dramatically change. AI analyzes digitized WSIs and identifies complicated morphologic patterns objectively, rapidly, and reliably. Here, we discuss the use of AI in histopathology, with a focus on precision medicine and its role in significant cancer diagnosis such as colorectal, lung and breast cancers. The book also discusses the computational techniques—such as convolutional neural networks (CNNs)—and whole-slide imaging systems behind these advances. AI has the potential to enhance diagnostics accuracy (up to 99%) and speed of slide assessment, while enabling telemedicine in parts without subspecialist expertise, yet a number of challenges remain. Data integrity, algorithmic reliance, cost control, and ethical or legal issues remain major problems. Ultimately, AI is one of the most important breakthroughs in modern pathology with unprecedented levels of precision, speed and personalized medicine.

Keywords: Artificial intelligence; Histopathology; Digital pathology; Whole-slide imaging; Deep learning; Convolutional neural networks

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1. Introduction

Pathologists are clinicians that perform analysis of tissues, cells and organs to ascertain a medical condition. This is important for doctors since they are greatly aid by this in identifying what type of illness it is and how it progresses; otherwise, targeted treatment plans cannot be formed. Two of the most recent technologies are artificial intelligence (AI) and digital pathology, which have revolutionized this field by improving diagnostic performance and workflow efficiency. These tools assist pathologists by handling routine and repetitive tasks, allowing them to focus on more challenging diagnostic questions [1]. AI, in particular machine learning and deep learning, has transformed aspects of histology. Data are collected through tissue preparation and histological staining, which can be subsequently evaluated by trained AI systems to recognize distinctive histological data that may go undetected by the human eye 6. Since the start of the twenty-first century, many countries including the United States, Germany and Britain were pioneering AI use in diagnostics. Thanks to their advanced healthcare

systems, these early adopters were able to show that vaccination was feasible and helped provide justification for widespread global adoption.

Iraqi Histology: A New Science Utilizing Artificial Intelligence While reliable reports about widespread employment of AI diagnostic technologies in the Iraqi healthcare centers are not yet prevalent, familiarity with their clinical benefits is beginning to grow. Research into artificial intelligence in medical diagnostics on both cancers and by academic and clinical investigators is accelerating across the nation, as major enterprises like Shanghai National Cancer Hospital explore application of AI to enhance diagnostic workflows and more efficiently deliver care. Moreover, the Warith Al-Anbiya Medical City at The Al-Husseiniya Shrine has also taken major steps to integrate AI technologies aimed at improving histopathology.

Simultaneously, creative uses of AI in digital pathology (especially used with Whole Slide Images or WSIs) are fuelling great advances in oncology. More studies are showing that AI models can detect the presence of various cancers and predict patient fate. On the other hand, simple detection has led to prognostic modeling among current capabilities in Artificial intelligence. For instance, advanced algorithms compute the five-year survival of a colorectal cancer patient and assess mutation signatures across different tumor types[1]. These advanced technologies improve diagnostic accuracy and contribute to personalized treatment planning by providing clinically relevant prognostic information. Most importantly, integrating AI in diagnostic pathology is a transformative step towards precision medicine for cancer and regimens with far reaching implications through further research that may lead to even greater breakthroughs in the form of patient care outcomes [2].

Many aspects of AI performance have been evaluated in various subfields of pathology. In 2020, Thakur et al. There were a total of thirty studies analyzing the potential of machine learning models for diagnosing colorectal cancer with each model demonstrating excellent diagnosis accuracy, but the overall volume of research available was limited in order to translate into therapeutic shnl. Similarly, Krithiga et al. assessed imaging research in breast cancer using image analysis techniques for detection, segmentation and classification and achieved diagnostic accuracies of 77–98% [2]. Additional assessments have examined AI use in liver, kidney, and dermatopathology with many models showing diagnostic promise. Second, in their comprehensive assessment of AI on whole slide images (WSIs), Rodriguez et al. We analyzed 26 studies focusing on slide-level diagnosis. In addition to the limitations in methods of existing literature, they discovered a high degree of heterogeneity in performance indicators. But their review was limited to evdience from other analytical units and a complete meta-analysis was not conducted. This work addresses these gaps by providing a comprehensive assessment of AI diagnostic accuracy across multiple digital pathology applications, focusing on studies with multiple analytic units[3].

2. Materials and Methods

This article employed a narrative review approach to synthesize evidence on the role of artificial intelligence in histopathological image analysis. The review was based on the scientific and clinical literature cited in the manuscript, including studies on digital pathology, whole-slide imaging, machine learning, deep learning, convolutional neural networks, cancer diagnosis, grading, prognosis, and AI-assisted workflow. The evidence was organized thematically into conventional histopathological workflow, transformation through digital pathology, disease-specific applications, whole-slide imaging requirements, convolutional neural-network approaches, and the advantages and limitations of AI-assisted diagnosis. Because this work is a narrative review rather than a systematic review or meta-analysis, the findings are presented as a qualitative synthesis and no pooled effect estimates were calculated.

3. Results

The reviewed literature revealed several consistent themes. Digital pathology and whole-slide imaging provide the infrastructure for converting histological specimens into

high-resolution data suitable for computational analysis [4], [5], [6]. AI-based systems have been applied to tumor detection, grading, segmentation, biomarker assessment, and prognostic modeling across several cancer types [7], [8], [9], [10]. Convolutional neural networks and related deep-learning methods are the dominant computational approaches for image classification, object detection, and segmentation [11], [12], [13]. AI-assisted systems may improve reproducibility and reduce time-consuming manual work, although performance remains dependent on image quality, training data, and external validation [2], [14]. Breast and lung cancer are among the most extensively represented clinical applications in the reviewed evidence [15], [16]. Implementation challenges include cost, interoperability, data standardization, legal and ethical responsibility, and the risk of over-reliance on automated outputs.

3.1. Traditional Steps of Histopathological Diagnosis

Disease diagnosis was largely dependent on the knowledge and careful study of qua lified pathologists prior to the application of artificial intelligence (AI) in the field of pat hology.

The diagnostic procedure had a number of organized steps that integrated clinical judg ment, laboratory equipment, and manual methods.An outline of pathologists' conventio nal diagnostic workflow is provided below [17]:

Sample Collection

The diagnostic process began with the collection of biological specimens from the patient. These samples varied depending on the suspected disease and could include:

a. Tissue biopsies
b. Blood samples
c. Urine
d. Cerebrospinal fluids or other body fluids

The quality and type of the sample played a crucial role in the accuracy of the final diagnosis.

Sample Preparation

Once collected, the samples underwent a detailed preparation process to make them suitable for microscopic examination. This included:

a. Fixation: The tissue was preserved using chemicals such as formalin to prevent degradation, however cytology samples usually preserved in alcohol.
b. Embedding and Sectioning: The sample was embedded in paraffin wax and then sliced into very thin sections using a microtome.
c. Staining: To highlight cellular structures, common stains like Hematoxylin and Eosin (H&E) were applied, which made the cells more visible under the microscope.

Microscopic Examination

The samples were then analyzed using secret slides in which the tissue was stained, to be view by a pathologist under a microscope. This was a complex process that required both skill and experience on the part of the pathologist:

a. Assess cell morphology (shape, size, and arrangement)
b. Detect Odd or Cancerous Cells
c. Identify changes in the architecture of tissues

It was mostly a diagnosis via visual interpretation and pattern recognition by the human eye.

Additional Tests

If the complementary histological study was not sufficient to reach a diagnosis, then other laboratory tests were performed, among them [17]:

a. Special Stains: It enabled the identification of particular microbes including fungi or bacteria.
b. Immunohistochemistry (IHC): Used antibodies to target specific proteins in the tissue, improving tumor classification or finding the origin of metastatic cancers.

c. Molecular Tests: PCR (Polymerase Chain Reaction) or FISH (Fluorescence In Situ Hybridization) were used to identify genetic mutations or chromosomal abnormalities.

Final Diagnosis

Based on the results from microscopic investigation and other tests, the pathologist would make a definitive diagnosis. This report included:

The first point is the name of the disease and another its type (e.g. cancer type).

The stage/grade of the disease (particularly important for tumors)

Prognostic information, if available

This was a meticulous process that demanded profound knowledge, nuance in precision and synthesis of complicated information.

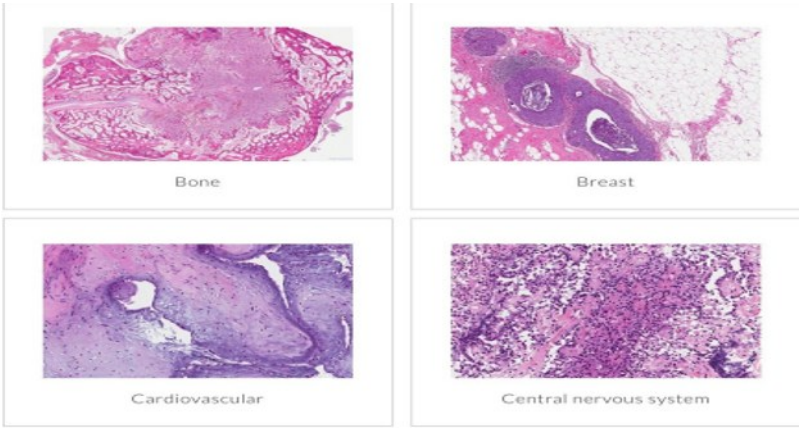


Figure 1. Traditional histopathological images of four tissue types (bone, breast, cardiovascular, and central nervous system), which pathologists relied on for diagnosis before the introduction of artificial intelligence techniques.

3.2. Impact of Artificial Intelligence on Histopathology

A. Transformative Shift

By contrast, incorporating artificial intelligence (AI) into histopathology is a paradigm shift in diagnostic practices. Since its inception, histopathology was largely based on the staunch visual examination of glass slides by a microscope; this method has been greatly affected by the indisputable judgment and prejudice of seasoned pathologists. This time-honored approach has been transformed with digital pathology and artificial intelligence [4], [18]. Digital pathology has become possible through whole slide imaging (WSI), which digitize pathology slides into ultra-high-resolution images that allow for sophisticated computerized evaluation. AI algorithms trained on these digital files can then be utilized to focus on very subtle histological features that would otherwise be overlooked [18]. AI often shows promise in improving diagnostic accuracy by recognizing complex patterns of tumor microenvironments, cellular morphology and tissue architecture. AI has reached performance levels that are often similar to and can sometimes outperform human experts in various diagnostic tasks, including cancer detection, tumor gradation, and metastasis foci discovery.

AI aids in greater accuracy and increased lab efficiency through the automation of repetitive tasks such as counting mitotic figures, detecting tumor margin and grading slides by complexity or priority. These technologies also serve a quality control function by identifying tissue artifacts or improper sectioning before pathology review [15]. The ability of AI to integrate digital imaging with clinical and molecular data is one of the unrecognized benefits from histopathology. Integration promotes precision medicine by ensuring prognoses and treatment plans that incorporate comprehensive histology as well as genetics specific to an individual patient. Even though AI has enormous potential, its implementation within routine pathology workflows poses several specific challenges. Top challenges include the need for large, well-annotated datasets, disparities in tissue preparation and staining practices among institutions, limited generalizability of models so far developed, and a lack of standard regulatory frameworks [15].

In summary, artificial intelligence has transformed histology into a data-driven, computational science rather than a primarily manual, visual field. Even if there are still a number of challenges, the continued development and application of AI technologies have the potential to significantly advance the field [5].

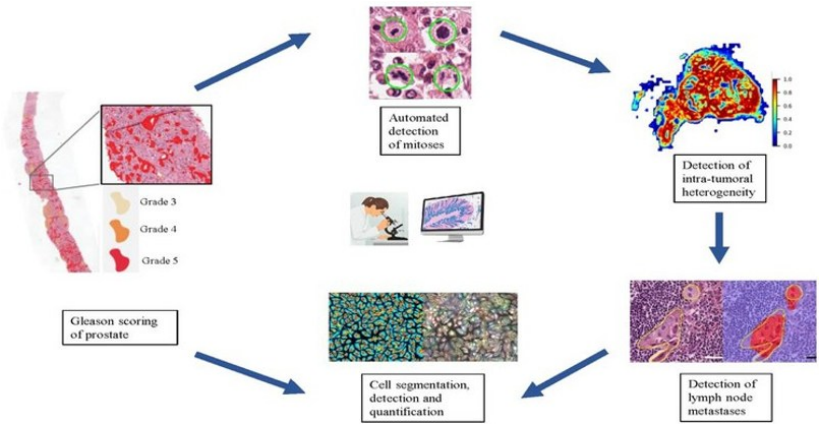


Figure 2. Depiction of artificial intelligence (AI) and machine learning approaches currently used by pathologists to analyze images from tumors [7].

3.3. Application of Artificial Intelligence in Disease Diagnosis

Several diseases and pathological areas where AI has been used are mentioned, including [5]:

Breast Cancer

a. Detection of mitotic figures for tumor grading.
b. Predicting gene expressions from histological images.
c. Survival prediction and disease progression.
d. Detection of metastasis in lymph nodes.

Lung Cancer

a. Evaluation of tumor-infiltrating lymphocytes (TILs) as immunological and prognostic markers.
b. Analysis of tumor patterns and prediction of clinical outcomes.

Colorectal Cancer:

a. Assessment of tumor-stroma ratio (TSR).
b. Use of topological tumor graphs to understand immune suppression.

Gastric Cancer

Survival prediction and genetic profiling.

Brain Tumors

Classification of tumor subtypes using unsupervised learning.

Prostate Cancer

Gleason grading and tumor classification

Prediction of tumor origin using only histopathology of metastatic sites.

Skin, Cervical, and Ovarian Cancers

In various contexts of diagnosis, classification, and prediction.

HER2 Status in Breast Cancer

Identified using H&E-stained slides alone.

3.3.1. Lung Cancer

In the US and around the world, lung cancer is the most common cause of cancer-related death. Making an accurate diagnosis is crucial for directing successful treatment planning since individual differences in disease development and treatment responses are significant. A key component of cancer identification is still microscopic examination of tissue slides, which calls for pathologists to recognize nuanced, subtle Histopathological patterns in complex tissue pictures. Nevertheless, this manual process is time-consuming,

subjective, and susceptible to significant fluctuation between and within observers. While radiology has long benefited from AI-assisted diagnoses, especially in identifying malignant pulmonary nodules and using CT scans to screen for early lung cancer [8], pathological tissue evaluation is still equally important. For example, the nodal (N) stage in the tumor, node, and metastasis (TNM) staging system [19] depends on examining pathology slides to ascertain whether a tumor has progressed to local lymph nodes. Finding tumor cells in dissected lymph nodes requires extremely specific knowledge and can be quite time-consuming, particularly when working with many nodes or tiny metastatic areas. By using computer-aided automatic tumor cell detection in lymph nodes, false-negative rates may be significantly reduced, early diagnosis and treatment can be advanced, TNM staging accuracy can be improved, evaluations can be completed more quickly, and pathologists' overall burden can be reduced [20], [21].

Pathology images provide important information about the tumor microenvironment (TME) that goes beyond tumor grades and subtypes [22]. Segmenting different tissue substructures and cell populations from these images is a fundamental step in quantitatively defining the TME. Subsequent analyzes, such as assessing cell composition, geographic distribution, and substructure-specific morphological features, require this segmentation. Tumor cells, lymphocytes, stromal cells, macrophages, and blood vessels make up the majority of the lung cancer TME. Studies show that whereas angiogenesis has a negative correlation with survival outcomes, tumor-infiltrating lymphocytes (TILs) are good prognostic indicators; stromal cells, on the other hand, have complex prognostic implications. Manual feature definition, extraction, and segmentation are commonly used in traditional image processing techniques [23], [24].

Predicting patient prognosis and treatment response using histopathological and morphological phenotyping to improve precision medicine is one of the most promising uses of digital pathology in oncology. Even as well-known pathological characteristics, including tumor grade and subtype, are acknowledged prognostic indicators, there is still much unrealized potential in the burgeoning field of directly linking raw pathology images to survival outcomes. Given that immunotherapy has shown promise for a portion of patients with non-small cell lung cancer (NSCLC), there are parallel opportunities to use pathology pictures to predict treatment efficacy [25].

Accurately predicting responses to immunotherapy is still a major clinical issue, despite the identification of multiple genetic biomarkers as prognostic determinants, such as PD-L1 expression and neoantigen load. The distribution of tumor-infiltrating lymphocytes (TILs) and the spatial organization of immune cells may have significant prognostic value for the results of immunotherapy. However, automated cell type identification and cellular spatial architecture characterization continue to be challenging issues in pathological image processing, requiring the development of sophisticated new algorithms [25].

The relationship between patient genetic profiles and clinical or morphological traits is the subject of another quickly developing field of study. This connection is essential for understanding the basic processes underlying the development of cancer and directing targeted treatments. Notably, many morphological characteristics and tumor genetic mutations, like EGFR and KRAS changes, have been found to be clearly correlated by researchers [26].

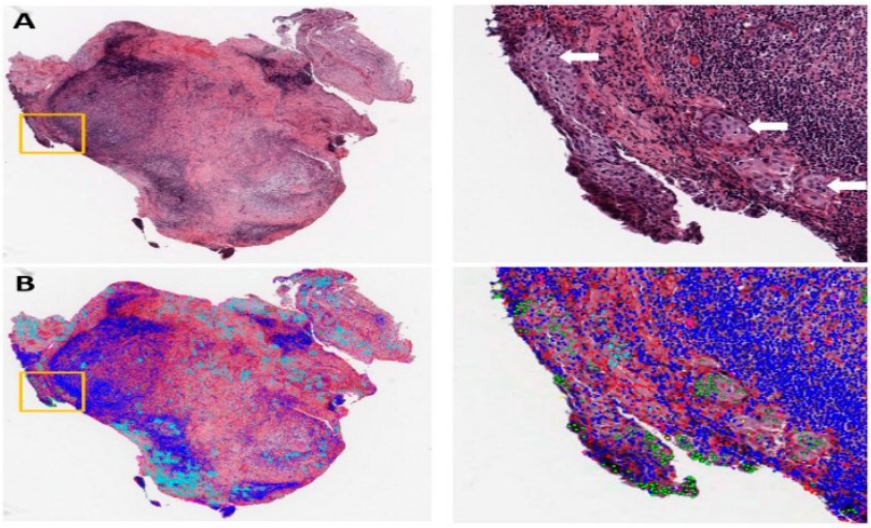


Figure 3. Example of metastasis detection in the lymph node for a lung adenocarcinoma patient. (A) Left: hematoxylin and eosin (H&E)-stained lymph node pathology slide (40×). Data were collected by the National Lung Screening Trial (NLST). Tumor cells began to invade into the capsule in the orange box. Right: region of interest in the orange box on the left, with white arrows pointing to tumor cells.
(B) Cell classification result overlaid on the H&E image. Green: tumor nuclei; blue: lymphocytes; red: stroma nuclei; cyan: necrosis

3.3.2. Breast Cancer

Breast cancer is one of the most prevalent and complex diseases in oncology. Because of its many subtypes and the unpredictability in treatment responses, accurate diagnosis, prognosis, and prediction of therapeutic results are essential for effective patient care. Microscopic inspection is still the gold standard for diagnosis, but it is constrained by variability between and within observers. The ability of histopathologists to provide more precise, reliable, and repeatable diagnoses has greatly increased with the advent of artificial intelligence (AI), machine learning (ML), and deep learning (DL) approaches.

Early identification of breast cancer can be facilitated by artificial intelligence algorithms that examine histological pictures and recognize patterns suggestive of the disease [27]. AI algorithms can precisely identify and segment cellular structures, such as nuclei, cytoplasm, and cell membranes, in breast cancer histopathology [16], allowing for quantitative evaluation of morphological aspects. Deep learning algorithms reduce inter-observer variability and promote diagnostic consistency by accurately classifying breast cancer into different histological grades and subtypes, much like skilled pathologists [28]. Additionally, immunohistochemistry biomarkers including estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67, which are essential for directing therapy choices, can be objectively quantified using AI-based techniques.

The increasing potential of AI in the pathophysiology of breast cancer has been shown by a number of research. Cruz-Roa et al. [29] and Fondón et al. [30], for instance, demonstrated how well AI can identify invasive ductal cancer in the surrounding breast tissue. In a similar vein, research by Han et al. [31], Yamamoto et al. [32], and Sharma and Mehra [33] found that deep learning models were remarkably accurate in classifying breast cancer. The capacity of AI algorithms to distinguish between benign proliferative lesions including both stromal and epithelial tissues and ductal, lobular, mucinous, and papillary breast cancer was further shown by Han et al. [31]. Furthermore, these algorithms were able to differentiate between ductal cancer in situ and atypical ductal hyperplasia.

One of the biggest problems in histopathology is the accurate classification of early-stage lesions with clear prognostic implications. AI solves this problem by correctly distinguishing between low-grade and high-grade in situ lesions, as well as between atypical ductal hyperplasia and ductal carcinoma in situ. Furthermore, by reducing observer variability and overcoming the time constraints associated with human assessment, AI has improved the reliability of mitotic figure detection.

Deep learning (DL) models have been applied to improve the stratification of intermediate Nottingham Histological Grade (NHG) 2 tumors, which have historically presented diagnostic and prognostic challenges due to their heterogeneity and intermediate clinical behavior. This has resulted in a significant advancement in breast cancer grading. These models, which closely resemble the traits of NHG 1 and NHG 3 lesions, are able to distinguish subtle morphological features that divide NHG 2 tumors into lower- and higher-risk categories by examining whole-slide histopathology pictures [34]. This approach provides prognostic information comparable to that obtained from molecular assays while offering advantages in terms of speed, cost-effectiveness, and reliance on routinely available Hematoxylin and Eosin (H&E)–stained slides.

Regardless of skill level, one of the most difficult and time-consuming jobs for histopathologists is still mitotic counting, a crucial part of breast cancer grading. The mitotic index is directly related to tumor aggressiveness and overall grade, and it is also linked to significant inter- and intra-observer variability. By eliminating observer-dependent variability and overcoming the time limits of manual assessment, artificial intelligence has greatly increased the accuracy and dependability of mitotic figure detection. Research by Li et al. [35] and Balkenhol et al. [36] showed that deep learning-based automated mitotic counting outperformed traditional manual techniques.

For the diagnosis of breast cancer, prognosis evaluation, and treatment planning, biomarkers must be evaluated accurately and objectively. The accurate measurement of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression is crucial for the efficacy of endocrine and targeted treatments. In recent years, a number of research teams have created artificial intelligence algorithms that perform on par with skilled histopathologists, exhibiting high levels of precision and reliability in the evaluation of ER, PR, and Ki-67 expression in breast cancer specimens [37], [38].

3.4. AI Techniques in Histopathology

Traditionally, pathologists use standard methods like Hematoxylin and Eosin (H&E) staining and other special stains to evaluate tissue sections under a microscope. Because histopathological interpretation mostly depends on subjective visual evaluation, pathologists may display both intra- and inter-observer variability despite their competence. Digital imaging is now a crucial part of computer-assisted pathology due to the introduction of computational ways to overcome these limitations. Among these technologies, Whole Slide Imaging (WSI) has become a more sophisticated and popular substitute for traditional static image acquisition techniques.

By digitizing whole stained glass slides into high-resolution panoramic images that retain cellular features and delicate tissue architecture, Whole Slide Imaging (WSI) enables precise and effective disease diagnosis. WSI's fundamental idea is built on the utilization of sophisticated scanners that take thousands of consecutive pictures at various focus planes. A seamless, high-definition virtual slide (VS) is then produced by stitching these images together. Virtual slides offer more versatility for research and diagnostic applications than traditional microscopy since they may be enlarged, annotated, stored, and analyzed using computational techniques.

There are currently a number of sophisticated WSI platforms available. The accuracy and high-throughput scanning capabilities of Leica Aperio systems are well known. While the 3DHISTECH Panoramic scanner offers complex image-processing capabilities and high-quality image acquisition, the Hamamatsu NanoZoomer scanner offers great picture resolution and quick scanning with many magnification settings. Digital pathology's capabilities are further expanded by software platforms like QuPath and Aperio

ImageScope, which enable automated quantification, image analysis, and the integration of AI-based diagnostic tools [5], [39].

3.5. Technical Requirements for Whole-Slide Imaging

The four main components of Whole Slide Imaging (WSI), a digital pathology technology, are picture acquisition, storage, processing, and display. Image capture devices and image display platforms are the two main integrated components that make up the hardware foundation of WSI systems. WSI makes it possible to create high-resolution virtual slides (VSs) by digitizing traditional glass slides. This allows for remote viewing, image analysis, and computer-assisted diagnosis.

1. Image Acquisition

Digital slide scanners, which operate as automated trinocular microscopes with robotic systems that control light intensity, stage movement, objective selection, and both coarse and fine focusing processes, are used to acquire images in WSI. Whole-slide scanners use either tile-scanning or line-scanning methods to obtain a sequence of consecutive images. A smooth virtual slide that faithfully replicates the original histology specimen is then created by stitching these separate images together.

2. Focusing Mechanisms and Image Resolution

Z-axis focusing, which enables picture acquisition at various focal depths and closely resembles the focusing process of traditional light microscopy, is used by WSI scanners to obtain best image quality. Focusing can be done on specific areas and reference points within the specimen or on each image tile separately, depending on the scanner design.

The scanning magnification is the main factor that determines the resolution of the created virtual slide. For the assessment of surgical pathology specimens and immunohistochemistry preparations, ×20 magnification is usually adequate in regular Histopathological practice. On the other hand, cytological specimens frequently need to be magnified by 40 times in order to offer the level of information required for precise assessment of cellular shape.

The diagnostic utility of WSI is further enhanced by the use of z-stack scanning, which captures many focal planes at different tissue depths, particularly in cytopathology. By revealing three-dimensional tissue architecture, Z-stack imaging improves the assessment of complex cellular features and increases diagnostic accuracy. Additionally, owing of their standardized preparation and staining methods, which lead to increased homogeneity and reproducibility, liquid-based cytology (LBC) preparations and cell blocks provide additional benefits. Previous studies on cervicovaginal cytology have demonstrated that ×40 magnification and z-stack scanning significantly improve diagnostic performance. This highlights how important it is to select the appropriate scanning parameters depending on the type of material. Additionally, better topographical analysis of cell layers enables intelligent sample selection based on cellular distribution patterns within the smear, increasing diagnostic accuracy and workflow efficiency [6].

3. Image Visualization and Software Applications

Whole slide imaging technology usually comes with specialized software packages that offer picture display, annotation, analysis, and export to several file formats. These software systems can be installed locally or hosted on network servers, depending on the intended clinical or research usage. Furthermore, many WSI platforms offer collaboration tools that make use of smartphones, tablets, and large touchscreen displays to enable remote consultation and real-time discussion during multidisciplinary meetings and scientific conferences. The application of digital pathology in clinical decision-making, research, and education has grown as a result of these qualities [6].

Table 2. Key Definitions of Terms in Artificial Intelligence and Computational Pathology

Artificial intelligence (AI)	The broadest definition of computer science dealing with the ability of a computer to simulate human intelligence and perform complicated tasks
Computational pathology (CPATH)	A branch of pathology that involves computational analysis of a broad array of methods to analyze patient specimens for the study of disease.
Deep learning	A subclassification of machine learning that imitates a logical structure similar to how people conclude using a layered algorithm structure called an artificial neural network
Machine learning	An artificial intelligence that parses data, learns from it, and makes intelligent judgments based on what it has learned.
Whole-slide image (WSI)	An whole histopathological glass slide digitized at microscopic resolution as a digital representation. Slide scanners are commonly used to create these complete slide scans. A slide scan viewing platform allows for image examination similar to that of a regular microscope.

3.6. Convolutional Neural Networks (CNNs)

Convolutional neural networks (CNNs) and image classifications, object detections, semantic segmentations CNN have proven their performance in medical image analysis. These deep learning architectures capture visual information hierarchically: from raw pixels to low-level patterns like edges and shapes to high-level representations of the most significant objects in medical images that can identify and classify complete images or distinct image components. Object detection: These methods, like you only look once (YOLO), or region-based convolutional neural networks (R-CNN), can be utilized to identify and locate certain anatomical structures or other abnormalities in an image. On the contrary, methods designed specifically for semantic segmentation such as Fully Convolutional Networks (FCNs) and U-Net enable pixel-wise classification and consequently a detailed representation of relevant structures and regions [35]. These methods have achieved great success, however directly applying them in the context of biomedical imaging is still challenging, particularly for analyzing gigapixel whole-slide images (WSIs). Pixel-level segmentation across entire WSIs can be computationally expensive and often unnecessary in histopathological tasks (e.g., tumor detection and tissue classification). To overcome this challenge, a sliding-window approach is often used in which large images are subdivided into small tiles to be processed independently. This approach generates superpixel-level masks instead of very fine pixel-wise segmentations. Superpixels represent a good tradeoff between accurate segmentation and computational efficiency, as they tend to be smaller than many of the most abundant histological structures [11]. While real-time processing is an important feature in many computer vision applications, computing speed may be less relevant in histopathology analysis, where manual annotation of tissue is inherently time- and labor-intensive. Deep learning development in recent years has shown that a data-driven automated techniques can classify histology images better and faster than by manual techniques. One such approach is Spatially Aware Histology Convolutional Neural Network (SA-HCNN), which uses Pyramid Tiling with Overlap (PTO) as a preprocessing step. PTO builds a pyramidal structure of overlapping image tiles across multiple resolutions, allowing the model to learn small-scale morphological details as well as large-scale tissue architecture. The SA-HCNN framework then processes the smallest tiles of this pyramid, enabling rapid and precise differentiation between patterns of pathology tissue [6], [11].

The architecture of SA-HCNN is built on the EfficientNetV2, a state-of-the-art convolutional neural network designed to optimize depth, width and image resolution of the networks together. On the other hand, EfficientNetV2 achieves strong classification performance whilst keeping computational efficiency by balancing these two traits. Deep

learning frameworks such as this one can potentially decrease the time needed for human image analysis [11] as well as integrating into digital pathology to automate histological annotation processes which are currently very labor intensive, thus increasing research throughput.

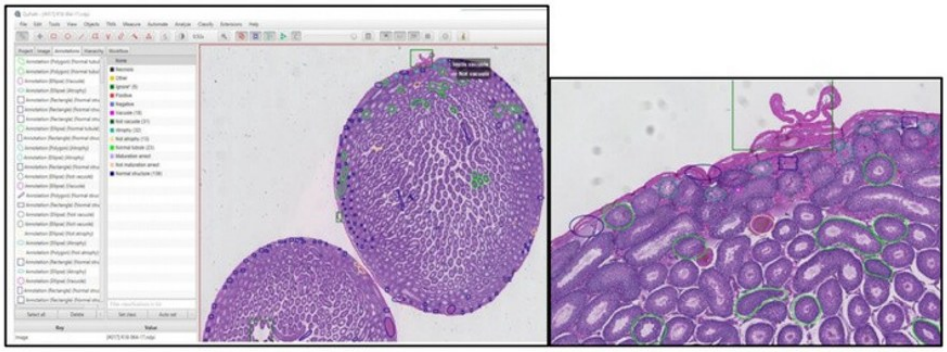


Figure 5. Example of a testis tissue image viewed in the QuPath system. Various regions of pathology have been human annotated in the image. The bottom image shows a zoomed in section from the top image that more clearly shows the annotations. For example, the light green annotations identify normal tubules, and the mid annotations identify atrophy. The large dark green rectangle annotates an "ignore" region

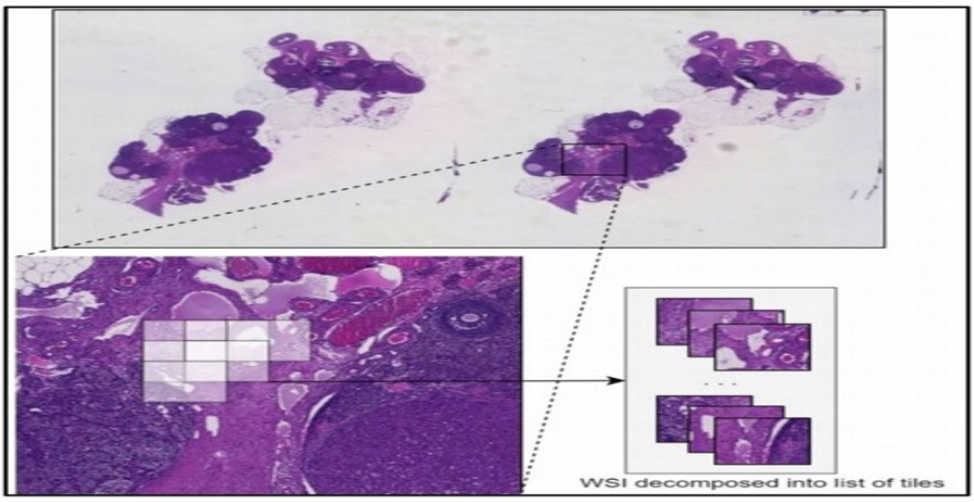


Figure 6. Illustration for tiling procedure on an ovary image. Tiles are extracted from the WSI using the sliding window approach with an increment of 128 pixels. To minimize computation time and memory usage, tiles which are mostly white are excluded from the tiled dataset.

3.7. Advantages and Disadvantages of AI Applications in Histopathology

A. Advantages

Artificial intelligence has significantly facilitated tasks for pathologists, enabling systems to assimilate all current diseases and distinguish between them with high accuracy. AI systems are capable of identifying rare diseases that human doctors might overlook, improving the diagnostic process significantly.

1. Diagnostic Accuracy:

The accuracy of AI systems in analyzing histopathological images has reached high levels, ranging from 92% to 99%. In some cases, the diagnostic accuracy of AI has been superior to human doctors, particularly in specific cases. However, the accuracy depends on several factors [40], [12]:

a. Disease type (e.g., breast cancer, lung cancer, skin cancer).
b. Quality of data used to train the system.
c. The type of algorithm used (e.g., Convolutional Neural Networks - CNNs).

d. Whether the system operates independently or assists the doctor.

For instance, it has been observed that AI analyzed breast cancer tissue slides with a diagnostic accuracy of 94.5%, compared to 88% to 96% among specialists. [40] Furthermore, Artificial intelligence accurately classified prostate cancer Over 87% on an independent dataset [12] in addition, some studies using deep learning techniques, the overall accuracy of tissue analysis reached between 93% and 98%, depending on the type of disease. [13].

However, despite its high accuracy, AI does not replace doctors; rather, it aids decision-making. In rare cases, AI may make mistakes in ways humans do not, making complete reliance on it without human review risky.

2. Speed of Diagnosis:

The time it takes for AI systems to analyze histopathological images varies depending on factors such as image size, device capabilities, and the AI model used. Certain systems have shown remarkable analytical speeds in spite of these differences. For example, the system can process a slide in about 0.27 minutes in high-throughput situations such as "OncoPetNet."[41] Similarly, tissue pictures can be examined in as little as 2.5 seconds each slide with "Slideflow" [42]. Additionally, a number of studies have indicated that AI support may enhance diagnostic effectiveness and maybe shorten the time needed for slide analysis in the pathology of prostate cancer.

3. Decision Support:

AI assists doctors in reinforcing decisions about treatment, thus reducing differential diagnoses.

4. Use in Remote Areas:

For example, there is a severe lack of expert doctors in a number of isolated and rural areas of Iraq, such as Anbar, Nineveh, Muthanna, and Diyala, especially in specialized fields like histology. There are several reasons for this shortage, such as the concentration of medical experts in large cities, poor healthcare infrastructure, and difficult security situations in some places. As a result, patients in these areas may encounter significant delays in obtaining precise pathology diagnoses, which may delay the start of suitable treatment, lower the possibility of early intervention, and perhaps raise morbidity and mortality. In this regard, a potential solution to the lack of specialist diagnostic knowledge is artificial intelligence (AI). Rapid and precise evaluation of tissue specimens can be supported by AI-based histopathological image analysis, which may lessen reliance on the prompt availability of local specialists. Tissue samples can be prepared, scanned, and electronically sent to an AI-based system for automated image analysis and diagnostic assistance in a digital pathology workflow. While lessening the burden on centralized hospitals in large cities, such technologies could increase access to specialist healthcare services in rural locations. AI-assisted diagnostic systems may also lead to better clinical outcomes and more prompt treatment by enabling the early detection of pathological anomalies. It is anticipated that these technologies will continue to develop in terms of accuracy, dependability, and future inclusion into standard histopathological practice [42].

Disadvantages

1. Over-reliance on AI

The possibility for an over-reliance on automated systems is one of the main issues surrounding the application of AI in medicine. Physicians can become unduly reliant on AI-generated outcomes and neglect to thoroughly assess or challenge the system's suggestions. When AI generates erroneous or deceptive results, this over-reliance may diminish the importance of clinical judgment and possibly lead to diagnostic errors.

2. Loss of Professional Motivation

Some pathologists' motivation to work may be impacted by AI systems' growing capacity to complete duties that have historically required years of specialized training. Some experts could feel that their work is less important or valuable if AI can analyze and interpret histopathological pictures in a matter of minutes. As a result, proper AI integration should highlight its function as a helpful tool rather than as a substitute for clinical judgment and expert knowledge.

3. Potential for Critical Errors

Although digital pathology systems coupled with AI technologies, such as automated pathology scanners, have shown great promise in the assessment of histological images, several potential sources of error and associated risks should be considered [14].

3.1. Imaging and Sample-Related Errors

Factors such as the quality of images, scanning conditions, and hardware calibration or miscalibration can cause errors in image acquisition process. These issues can cause images to be cropped, misaligned or unclear reducing the quality for subsequent analysis by AI Business1. In addition, since AI systems are often trained on more standardised datasets, force differences in tissue preparation, staining procedures and specimen quality may actually impact model performance negatively.

3.2. Processing and Diagnostic Errors

AI systems may make mistakes when they analyze rare diseases or specimens that are very different from the data with which models were trained. This limitation can mitigate the generalizability of AI-based diagnostic systems covering a wide range of populations, labs, and disease states. Also, an AI algorithm might predict incorrectly, but do so with overconfidence such that the clinical meaning of the output is a definitive diagnosis even when not explicitly conveying uncertainties about the outcome.

3.3. Software and Technical Errors

When AI systems deal or integrate with hospital management platforms and laboratory information systems, technical problems or software related problems may also arise. Such failures may lead to inappropriate processing, delays in diagnosis, or loss of critical information from imaging and clinical records [14]. Even in digital pathology, humans can introduce errors as they physically handle the slides, prepare specimens, photograph specimens, and interact with the digital pathology instru- ments. While AI technologies offer immense potential, ensuring safe implementation will require careful quality-control protocols, continuous monitoring of systems, appropriate oversight levels for health care professionals in both development and use of the system, as well as frequent validation and updating of the models used to support diagnostic accuracy and reliability across the spectrum of standard clinical practice.

4. High Acquisition and Maintenance Costs

The costs associated with purchasing, setting up, maintaining and continuously advancing systems at healthcare organizations can be massive. AI-enabled digital pathology scanners vary considerably in price depending on the make and model, technical specifications, scanning capabilities, and additional functionality. The systems themselves run $70,000 to $100,000 which can be a considerable barrier to entry for most health systems with limited resources.

5. Legal and Ethical Challenges

The use of AI in medical diagnosis also raises questions of ethics and legality. In Iraq, the law punishes medical mistakes — particularly diagnostic errors depend on its seriousness and type, then doctors may be legally accountable for these kinds of mistakes [19]. Now, this might prove problematic when AI comes into play of the misdiagnosis that lead to death, great bodily injury or any kind of permanent impairment for legal culpability. These kinds of cases bring up questions over who shares responsibility; the doctors, hospitals, and even AI developers and what should be share to tech-makers. Thus, regulatory frameworks with clearly defined roles will be required to enable safe and legal real world use of AI in histopathology.

4. Discussion

The synthesis indicates that the principal contribution of AI to histopathology is not simply faster image processing, but the conversion of tissue morphology into analyzable digital data that can support more reproducible diagnostic decisions. Whole-slide imaging provides the infrastructure for this transition, while machine-learning and deep-learning models extract patterns related to tumor presence, grade, tissue architecture, and prognostic features [4], [5], [6]. This is particularly relevant because conventional

histopathological interpretation depends heavily on expert visual assessment and may be affected by inter- and intra-observer variability.

The strongest clinical evidence discussed in this review concerns oncology. In lung cancer, computational pathology can support lymph-node metastasis detection, tumor-microenvironment characterization, and relationships between morphology and clinically relevant molecular features [8], [9], [20], [21], [22]. In breast cancer, AI has been applied to invasive tumor detection, histological classification, mitotic counting, biomarker assessment, and refinement of intermediate-grade tumors [27], [16], [29], [31], [34], [36], [37], [38]. These findings suggest that AI is most useful when it augments specific, well-defined diagnostic tasks rather than attempting to replace the complete interpretive role of the pathologist.

At the technical level, convolutional neural networks remain central because they can learn hierarchical visual features directly from histopathological images. However, whole-slide images are extremely large, making direct pixel-level analysis computationally demanding. Tiling, weak supervision, and scalable deep-learning strategies therefore provide practical solutions for clinical-scale analysis [11], [12], [13]. Even so, high internal accuracy does not guarantee clinical generalizability. Differences in staining, scanners, specimen preparation, patient populations, and annotation quality can substantially affect model performance, reinforcing the importance of external validation and continuous quality control [14].

Clinical adoption also requires attention to human and organizational factors. High diagnostic accuracy and rapid processing may improve workflow and extend specialist support to underserved settings, but over-reliance on algorithmic output could weaken independent clinical judgment. Acquisition and maintenance costs, integration with laboratory information systems, privacy, accountability, and medico-legal responsibility remain important barriers. The evidence therefore supports a human-in-the-loop model in which AI functions as decision support under pathologist oversight. Future studies should prioritize multicenter external validation, standardized digital-pathology workflows, transparent reporting of model uncertainty, and prospective evaluation of clinical outcomes rather than diagnostic accuracy alone.

5. Conclusion

Artificial intelligence (AI) has transformed histopathology by enabling the shift from traditional human-controlled diagnostic workflow to automated data-driven pathways. Again, there are many cancers that have a strong histopathological basis for their identification, classification and characterization; which has been made possible by advanced digital image analysis and deep learning methods allowed in the presence of artificial intelligence based imaging systems for providing improved prognostic assessment as well as diagnostic accuracy.

Integrating AI into the routine practice of histopathology may have the potential to improve workflow efficiency, reduce inter-observer variability and assist in early diagnosis especially in remote/resource limited settings where access to specialty-based pathology services is less available. Nevertheless, there are many technical, legal and ethical issues that still block the use of AI in practice. These pertained primarily to data quality and lack of standardisation, interpretability of models, external validation and ambiguity on who is professionally and legally responsible. Thus the way forward is to consider AI as an auxiliary or a complementary augmentation tool that serves to augment and complement human expertise to support pathologists in effective clinical decision making rather than replacing them. The required advances will arise through ongoing research, extensive validation, harmonization of data practices and optimal regulatory path forward to enable the safe and effective implementation of AI into daily practice of histopathology. Which in return would facilitate more reliable, precise and patient-centered diagnostic health care.

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