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PERSPECTIVES ARTICLES

Artificial Intelligence in Pathology: Past, Present, and Future Perspectives

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Abstract

Introduction: Artificial intelligence (AI) is at the forefront of modern technology, with emerging applications in the healthcare sector now gaining recognition. Pathology is anticipated to be a key area where the impact of AI will be substantial. As more laboratories transition to digital pathology, this will create the essential infrastructure needed to implement these tools, making their application a reality in diagnostic practice. The potential of AI in pathology lies in developing image analysis tools that can support diagnosis or generate new insights into disease biology, beyond what a human observer can achieve. Examples currently exist providing diagnostic support for a limited but growing number of applications, such as tumor detection, automated tumor grading, immunohistochemistry scoring, and predicting mutation status. Several challenges remain, including the validation and establishment of a regulatory framework for these tools, as well as the ethical implications of AI in pathology. These include concerns about patient privacy and consent, along with the potential for AI to worsen existing healthcare disparities. In this article, we offer an overview of AI in histopathology, discuss its possible workflow applications, and highlight significant examples of AI's potential impact in clinical practice. We also explore considerations for implementing AI in practice.

Conclusion: There has been a significant increase in the development and application of AI tools, including image-based algorithms, in pathology services, and they are expected to dominate the field in the coming years. The implementation of computational pathology and the use of pathology-related AI tools can be viewed as a paradigm shift that will transform the management of pathology services. While AI will undoubtedly enhance the efficiency of pathology services, it is crucial to recognize that it will not replace the role of pathologists. Instead, it will augment their capabilities, enabling them better to meet the demands of this era of precision medicine.

Keywords: Artificial intelligence (AI), digital pathology, tumor grading, immunohistochemistry, histopathology

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Introduction

Artificial intelligence (AI) is at the forefront of modern technology, and emerging uses within the healthcare sector are now being realized. Pathology will be a key area where the impact of AI is expected to be felt. As more laboratories transition to digital pathology, this will provide the key infrastructure to deploy these tools, and their use will become a reality in diagnostic practice. The potential of AI in pathology lies in creating image analysis tools that can either support diagnosis or derive novel insights into disease biology, in addition to those achievable by a human observer. [1]

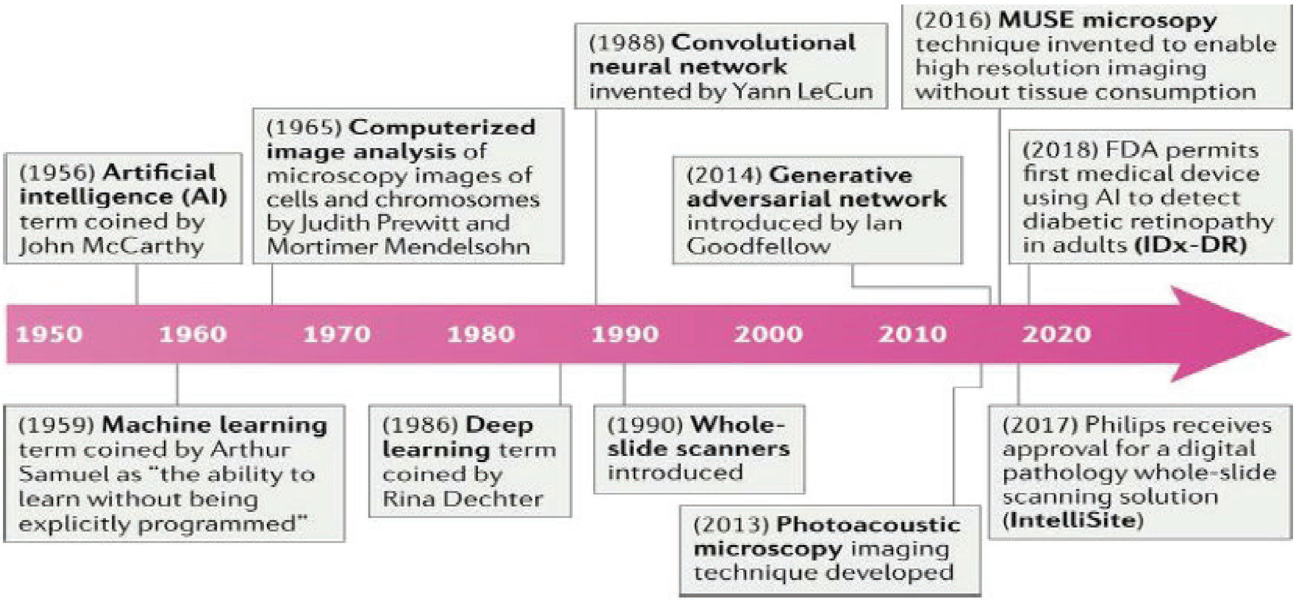
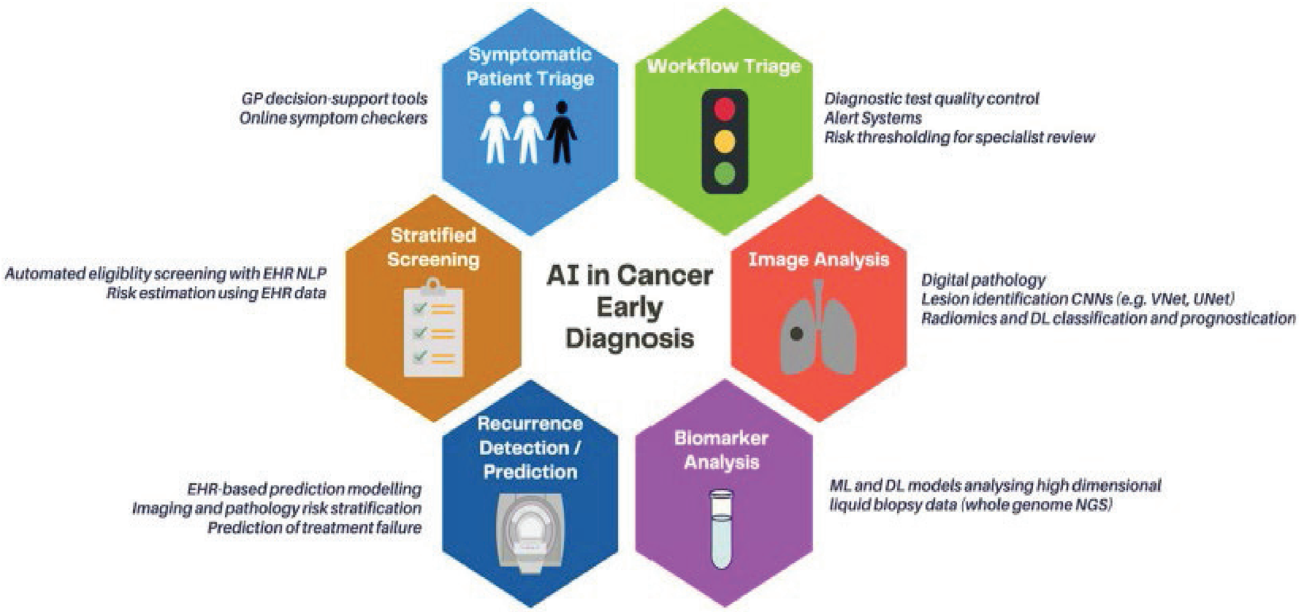


Figure 1 AI in pathology over the years

Over the past two decades, technological advances have enabled the efficient digitization of whole-slide images, helping to streamline pathology workflows across pathology labs worldwide. Slide digitization has facilitated the creation of large-scale digital slide libraries, the most notable of which is probably The Cancer Genome Atlas, allowing researchers worldwide to freely access a richly curated and annotated dataset of pathology images linked to clinical, outcome, and genomic information. This, in turn, has spurred substantial research activity in artificial intelligence for digital pathology and oncology [2].

Current Applications of AI in Pathology

AI applications in pathology diagnosis can encompass rare and complex cases that often pose challenges for general pathologists, who seldom encounter them. AI can search for images similar to query images from extensive histopathological databases, a process known as content-based image retrieval (CBIR). CBIR enhances the pathological diagnosis process by increasing the likelihood of achieving a correct diagnosis for complex cases through the rapid retrieval of similar cases from available



GP: general practitioner, NLP: natural language processing, EHR: electronic healthcare record, ML: machine learning, DL: deep learning, NGS: next-generation sequencing. [3]

Figure 2. Clinical applications of AI in early cancer diagnosis.

pathological image databases that contain such rare and complex instances. Here, similarity refers to the associated histopathological features rather than mere image similarity. Other applications of AI in pathology include automated tumor grading, immunohistochemistry scoring, and predicting mutation status.

Standard Workflow of AI-assisted Renal Pathology

The standard workflow for conducting an AI-assisted renal pathology study typically consists of four stages:

(i) problem definition,
(ii) data collection and annotation,
(iii) AI development and training,
(iv) data fusion and analysis. With fine-grained classification, AI can determine the percentage of glomeruli with global glomerulosclerosis (GS).

Renal Pathology–Optimized Deep Learning

Currently, most AI-assisted renal pathology studies utilize off-the-shelf deep learning algorithms developed in the computer vision community, such as Faster R-CNN, Mask R-CNN, and U-Net. The rationale is that renal pathology and computer vision fields handle similar targets—images. Therefore, applying widely used computer vision algorithms to renal pathology is a natural and reasonable choice. [5]

Pathology Image Analysis Using Segmentation Deep Learning Algorithms

Optical microscopy of pathology slides captures the histologic details of tissues in high resolution. With the rapid advancement of technology, whole-slide imaging (WSI) is becoming a routine procedure for diagnosing various diseases. The emergence of digital pathology[6, 7] provides new opportunities to develop algorithms and software tools to assist pathologists in clinical diagnosis and researchers in studying disease mechanisms. Digitalized pathology slides are often referred to as images in the computer vision field and can benefit from various image analysis algorithms. For example, pathologists can also achieve the common task of locating and recognizing tissue components through image segmentation and recognition algorithms.

Currently, digital pathology is advancing rapidly thanks to the success of deep learning. Due to its high complexity, digital pathology had limited success with labor-intensive modeling before the advent of deep learning algorithms.

Since 2012, deep learning has significantly improved all image recognition benchmarks.[8, 9, 10] The applications of deep learning algorithms in digital pathology have achieved remarkable success in traditional pathology tasks. For instance, deep learning algorithms have demonstrated performance comparable to that of pathologists in interpreting whole-slide images for detecting tumor regions and lymph node metastases. Although this comparable performance may not generalize to all task domains, advanced methodologies are expected to address or assist with common challenges that pathologists encounter, such as locating neoplasia within tissue and quantifying specific features, including mitoses and inflammation.[11]

The Role of Artificial Intelligence in Early Cancer Diagnosis

Early cancer diagnosis and artificial intelligence (AI) are rapidly evolving fields with significant areas of overlap. In the United Kingdom, national registry data suggest that cancer stage is closely correlated with 1-year cancer mortality, showing incremental declines in outcomes with each stage increase for some subtypes. Using lung cancer as an example, the 5-year survival rates following resection of stage I disease range from 70% to 90%; however, the overall rates are currently 19% for women and 13.8% for men. In 2018, the proportion of patients diagnosed with early-stage (I or II) cancer in England was 44.3%, with lower proportions than 30% for lung, gastric, pancreatic, esophageal, and oropharyngeal cancers. A national priority to improve early diagnosis rates to 75% by 2028 was outlined in the National Health Service (NHS) long-term plan. Internationally, several organizations recognize early diagnosis as a key priority, including the World Health Organization (WHO) and the International Alliance for Cancer Early Detection (ACED).

Numerous studies suggest that screening can improve early cancer detection and reduce mortality. However, even in disease groups with established screening programs, such as breast cancer, ongoing debates persist regarding patient selection and risk-benefit trade-offs. Additionally, concerns have been raised about a perceived 'one size fits all' approach that is inconsistent with the goals of personalized medicine. Patient selection and risk stratification present significant challenges for screening programs. AI algorithms, capable of processing vast amounts of multimodal data to identify signals that are otherwise difficult to detect, may play a significant role in improving this process shortly. Moreover, AI has the potential to facilitate cancer diagnosis directly by prompting further investigation or referral for individuals screened based on clinical parameters, and by automating clinical workflows where capacity is limited. In this review, we discuss the potential applications of AI for early cancer diagnosis in both symptomatic and asymptomatic patients, focusing on the types of data that can be employed and the clinical areas most likely to experience impacts soon. [12]

Challenges in the adoption of AI in pathology

The promise of healthcare AI presents several challenges, including ethical considerations, algorithmic fairness, data bias, governance, and security. Developing ethical principles and frameworks is a significant area of ongoing work in healthcare AI. The WHO has called on healthcare AI stakeholders to ensure that new technologies prioritize ethics and human rights in their design and use.

The first challenge is conceptual and cultural, as the adoption of AI in pathology necessitates two fundamental paradigm shifts: the introduction of digital pathology for cancer diagnosis and assessment, along with the transition from a human-based diagnosis or assessment system to one in which AI will render the final diagnosis or provide the ultimate results for a given biomarker. New technologies require the discontinuation of established practices, which can cause distress for users. For instance, the introduction of microscopes for diagnosing and characterizing diseases was met with significant resistance from physicians, best exemplified by the notable microscopy debate at the Paris Academy of Medicine in the 19th century. Similarly, the move from traditional microscopes to routine digitalization of glass slides has been successful in only a few institutions in the 2010s, yet it still faces widespread resistance. Even the initial step for digitalizing pathology—transitioning from a traditional histology workflow to a "radiologist-like" workflow where the user reviews images on a computer screen—is still not a reality. Indeed, why should pathologists shift from microscopes to computer screens if the current workflows are cost-effective and efficient, and the training of new pathologists predominantly relies on microscope-based diagnoses? Digital pathology measuring tools and

Remote work provides strong incentives, but the ultimate motivator could be the development of AI-based biomarkers. Once clinical evidence supports the predictive and prognostic power of these biomarkers and clinical guidelines recommend AI biomarkers, pathology departments will inevitably need to digitize; otherwise, assays essential for patient care will not be accessible. Therefore, evaluating and validating AI biomarkers in samples from prospective clinical trials will likely act as a catalyst for the digitalization of histopathology. However, access to the algorithms being developed is restricted, given the limited digitalization of pathology. In countries such as Sweden, the United Kingdom, and the Netherlands, large-scale efforts are underway or have been completed to digitize most major pathology departments. In many other countries, the digitalization of pathology is not yet a national priority and has not commenced on a large scale.

The perspective of the pathologist

For a pathologist, AI-based tools will primarily be needed to detect specific structures or regions of interest in digitized whole-slide images (WSIs). Thus, the digital slide scanner is a critical element in developing such applications, as it enables quick turnaround times and the ability to control the clinical workflow. Moving forward, as slide scanners become more widespread in hospitals and medical institutions, the deployment of AI tools may be app-based, integrating into the data cloud to allow pathologists to instantly share images and AI-generated predictions with collaborators and patients worldwide. Current challenges associated with cloud-based usage include the substantial bandwidth required to transmit gigapixel-sized WSI images to data clouds and managing

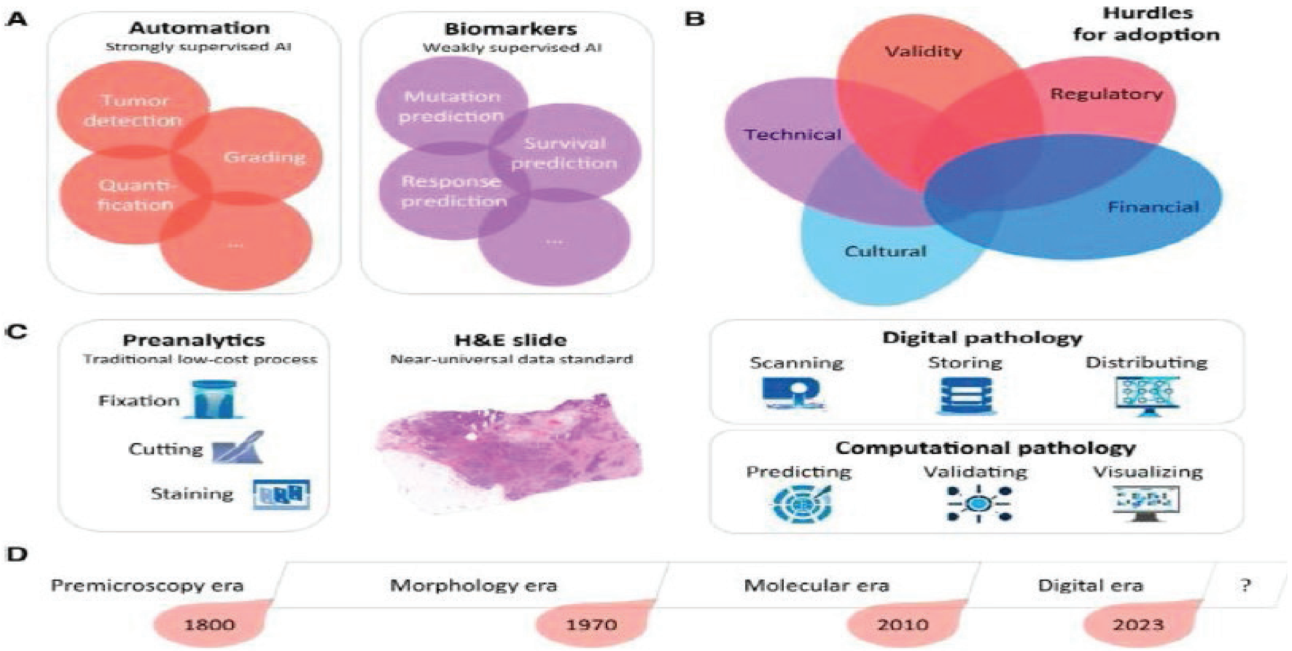


*Figure 3: History, potential, and challenges of computational pathology: **A)** Key use cases of artificial intelligence (AI) in pathology. Intensely supervised AI has mainly been used for diagnostic purposes or to generate input data for downstream prognosis or treatment response models. Weakly supervised AI can directly yield diagnosis, prognostic, or predictive models. **B)** Challenges of AI in histopathology. **C)** Histopathology workflows in the AI era. **D)** Simplified timeline of developments in histopathology. H&E: Hematoxylin and eosin. [15]*

permanent and uninterrupted communication channels between end users and the cloud. Another consideration regarding the transition to digital pathology is the potential for automated approaches to assess the quality of digital slide images. Computerized algorithms, such as HistoQC and DeepFocus, have been developed in recent years to standardize the quality of Whole Slide Images (WSIs). These tools can automatically evaluate and detect optimal quality regions for analysis, while eliminating out-of-focus areas and those with artifacts. [14]

Conclusion

There has been a sharp rise in the development and application of AI tools, including image-based algorithms, in pathology services, and it is expected to dominate the field in the coming years. The deployment of computational pathology and the use of pathology-related AI tools represent a paradigm shift that will transform how pathology services are managed, making them more efficient and capable of meeting the demands of the precision medicine era. Developing pathology-based AI tools requires input from a multidisciplinary team, where pathologists and users play a significant role in enhancing the adoption of these technology-driven applications. Integrating AI with pathologists can yield more accurate, consistent, timely, and valuable results that exceed human capabilities. AI can offer analytical tools to streamline the complex, multistep case life cycle in pathology laboratories, from accession to archiving.

This can provide not only workflow automation but also an analytics dashboard and data repository that enhance efficiency by self-learning from previous experiences, helping to understand laboratory productivity, quality, and efficiency, while also assisting in allocating future resources to areas in need. AI can further streamline the entire process by aligning the laboratory's technical components of the case pathway with the pathologists' reporting components.

Enhancing the efficiency of pathology service workflow, the reporting of trainee and junior pathologists, timely reporting by pathologists, cost-effective diagnostic and prognostic/predictive algorithms, and the production of comprehensive pathology reports, along with the integration of imaging and genomic data, are some of the anticipated benefits of applying AI technology in routine practice.

AI applications will also pave the way for advanced diagnostics, enabling researchers and clinical teams to share knowledge and utilize computational algorithms to evaluate and provide valuable insights, ultimately leading to a more informed and comprehensive pathology diagnosis. This integration will help advance the future of precision oncology and may lead to more personalized care plans. [16]

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Abbreviation

AI - Artificial intelligence; GP - General Practitioner; NLP - Natural Language Processing; HER - Electronic Healthcare Record; ML - Machine Learning; DL - Deep Learning; NGS - Next-Generation Sequencing; CBIR - Content-Based Image Retrieval; GS - Global Glomerulosclerosis; WSI - Whole Slide Imaging; NHS - National Health Service; WHO - World Health Organisation; ACED - Alliance for Cancer Early Detection; H&E - Hematoxylin and Eosin.

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