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PAPER

# Digital Pathology in Healthcare: Current Trends and Future Perspective

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**ABSTRACT**

Diagnosing a disease requires observing the affected tissues and drawing conclusions based on specific known features. Conventionally, a pathologist would diagnose the sample manually by placing it on a glass slide and viewing it under the microscope. These microscopes existed 400 years ago, but over the years, there have been modifications aimed at digitizing every possible diagnostic test. One of the major advantages of digitizing the process is the reduced time consumption for acquiring, processing, and analyzing the slides. Another positive aspect is the reduction in subjectivity achieved by utilizing artificial intelligence (AI) algorithms to classify and diagnose specific diseases. This is achieved by attaching a digital camera to the microscope, which captures images of the glass slides for subsequent processing and diagnosis. There has been a lot of research in this field, but its implementation has been hindered by challenges such as interoperability and high-resolution data, resulting in large file sizes. Various applications for whole slide imaging, such as disease diagnosis techniques, whole slide imaging (WSI) scanners, digital slide scanners, the Internet of Things (IoT), and AI, have been explored in this study. This paper reviews the trends and evolution of microscopes leading to present-day digital pathology scanners, with a major focus on one of the digital techniques, which is whole slide imaging. It also explores various areas where AI has been integrated into whole-slide imaging.

**KEYWORDS**

whole slide imaging (WSI), image analysis, artificial intelligence (AI), pathology

## 1 INTRODUCTION

Digital pathology involves acquiring pathology slides from a hospital, reporting them, sharing them between hospitals, and storing and managing them. Digital pathology is a field of pathology that utilizes digital images of biological samples to study and diagnose diseases. It has several advantages over conventional microscopy, including faster, more accurate, and more reliable diagnoses; better access to specialist advice; improved patient care; enhanced education and training; and the ability to store and share large datasets. It utilizes a digital microscope with a

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digital camera to capture the image, which is then displayed on the computer screen for storage, editing, and analysis. It is different from the conventional approach in terms of time, efficiency, and accuracy. These digital images are obtained through whole-slide imaging (WSI) technology, where glass slides are scanned to generate digital images. Digital pathology enables the transmission of WSI data electronically from one hospital to another through high-speed digital lines, satellites, the Internet, or any other communication medium [1]. This feature is used for telepathology. To perform telepathology efficiently, the pathologist selects a video image for diagnosis. Both real-time and static images are transmitted simultaneously in hybrid telepathology [2]. A remote location or primary care center can upload digital images to a web browser for access from anywhere in the world. Specialized pathologists can virtually report and provide expert opinions on digital images of slides. For transferring them over the network, they need to be standardized. The standard for medical images is DICOM, while the standard for information is HL7. The evolution of microscopes started in the 14th century, and it took six centuries to reach the digital era. Table 1 describes the evolution of modern-day microscopes, including their inventors and advancements [3, 4, 5, 6, 7].

Whole slide imaging technology emerged in 1999 [8], which allowed pathologists to digitally convert all the tissue on the glass slide into a virtual slide with higher resolution [9]. There are four processes involved: image acquisition, storage, processing, and visualization. There are several modes of digital pathology, including static mode, dynamic mode, and hybrid mode [10]. In all these modes, whole-slide images were included. Static modes were used in transplantation using a private network and client-server architecture. In hematopathology, static images of blood cells were transmitted via email from one place to another [11].

**Table 1.** Evolution of digital microscope

| Century | Inventor | Progress |
|---|---|---|
| 14th Century | Roman Philosophers | The invention of a microscope, which could concentrate sun rays into a small area. |
| | | Two lenses were set on opposite sides, leading to a simple magnification tube. |
| 16th Century | Dutch lens makers | A device that could magnify objects |
| | Galileo Galilei | Complete microscope, i.e., today's simple microscope |
| Mid-16th Century | Zacharias Jansen and Hans Lipherhey | Created microscope based on lenses in a tube |
| Late 16th Century | Anton Von Leeuwenhoek | Started polishing the lens and also measured which would be of good quality |
| 18th Century | Chester Moore Hall | Made the achromatic lens |
| 19th Century | Charles Spencer | Observed how light affects the image in the microscope and later developed an independent light microscope |
| | Ernst Liedst | Different magnifications in a microscope |
| 20th Century | Maxx Roll and Ernst Rucher | Invention of the electron microscope |
| | Gerard Benign | Scanning tunnelling microscopy and atomic force microscopy |
| | | Digital Microscopes |

Whole-slide imaging technology, also known as virtual microscopy, scans and captures the entire microscopic slide using a camera to produce a high-resolution image [12]. It follows the Pixel Pathway process, which traces the flow of image data from a glass slide to a human. These static images provide us with relatively more data on magnification and its focal planes. The time required for this process is very short. After the acquisition of the pathological image data, it is stored on an SD card or in the cloud and then viewed using a virtual slide viewer [13]. Figure 1 illustrates the fundamental workflow of the WSI process.

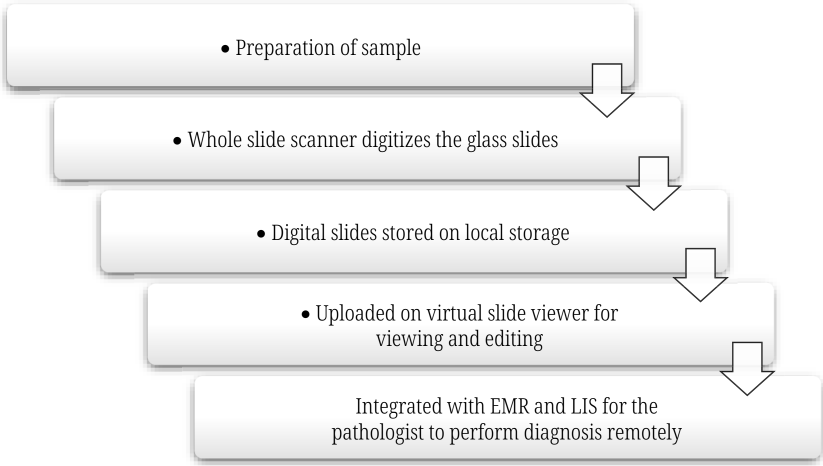


**Fig. 1.** WSI workflow

To initiate the process of acquiring WSI, various magnifications need to be taken into consideration. The basic concept of light microscopy is different from the one used in WSI because of the objective used to scan the slide and the imaging sensor [14]. The most widely used magnifications are 20× with a resolution of 0.5 µm per pixel and 40× with a resolution of 0.25 µm per pixel [15]. Figure 2 shows whole slide images of a human esophagus at different magnifications.

Under the same umbrella, there have been other review papers as well. "AI and Digital Pathology: Challenges and Opportunities [16]" and "Image Analysis and Machine Learning in Digital Pathology: Challenges and Opportunities [17]" are two articles that discuss the current state and future potential of using AI in the field of digital pathology. Both papers highlight the benefits of digital pathology, such as improved accuracy, efficiency, and accessibility of pathology services. It also notes that there are several challenges that need to be addressed, such as data privacy, lack of standardization, and the need for extensive training data sets. Along with this, Amerikanos *et al.* [17] also discuss various image analysis and machine learning techniques that have been applied to digital pathology, such as convolutional neural networks (CNNs), deep learning, artificial neural networks (ANNs), and different types of applications of these techniques in digital pathology, including diagnostic support, disease prognosis, and treatment planning. WSI is a part of digital pathology that digitizes high-resolution digital images of entire tissue samples, which can be viewed and analyzed using specialized software. [18] is another review paper that delves into past experiences with digital pathology implementations, explores future possibilities with the integration of AI, addresses technical and occupational health challenges, and considers potential changes to the pathologist's profession.

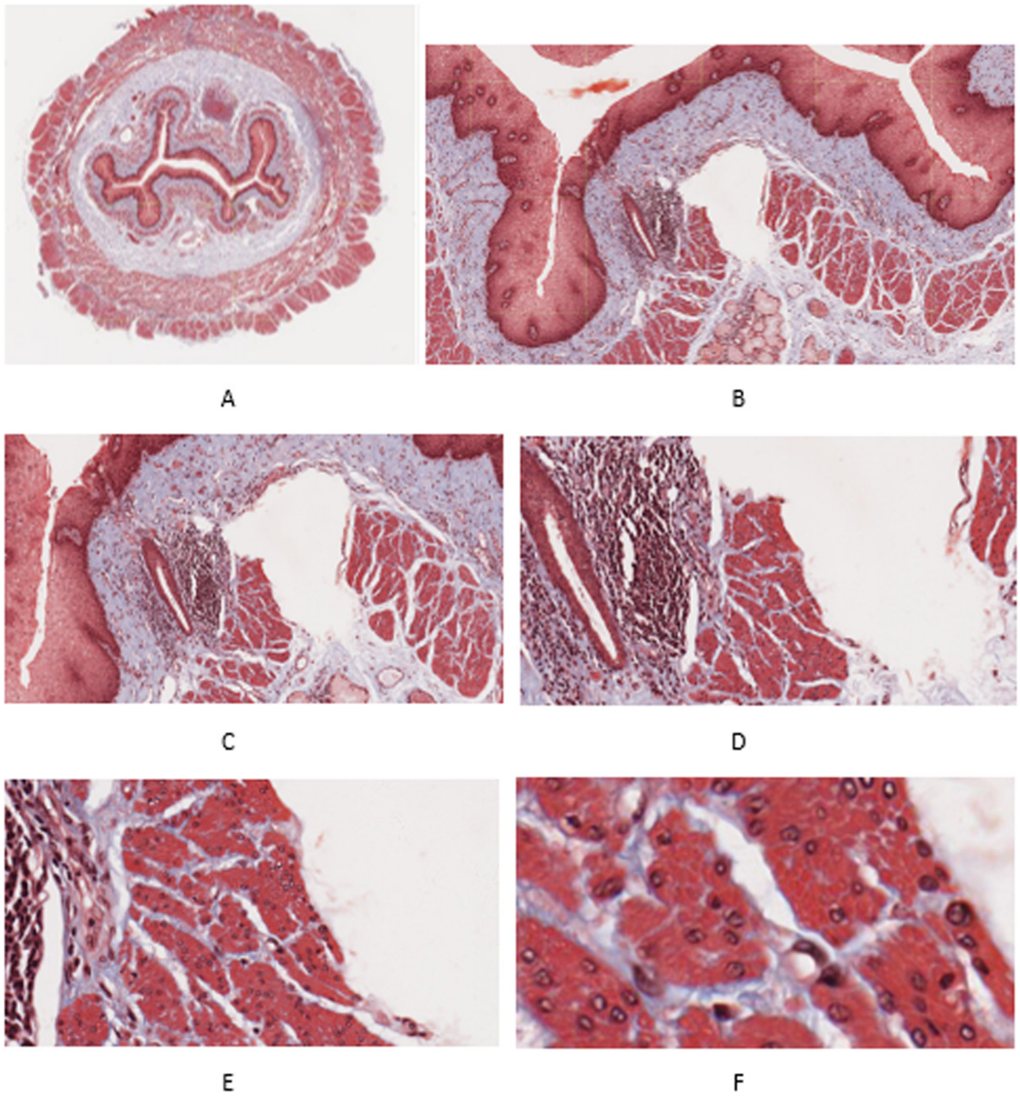


**Fig. 2.** Whole slide image of human oesophagus. A) Whole slide image viewed at 0× magnification. B) Whole slide image viewed at 5× magnification. C) Whole slide image viewed at 10× magnification. D) Whole slide image viewed at 20× magnification. E) Whole slide image viewed at 40× magnification. F) Whole slide image viewed at 80× magnification [19]

Whole slide imaging: technology and applications [20] and WSI in pathology: advantages, limitations, and emerging perspectives [21] review the same topics, highlighting the benefits of WSI technology, including enhanced diagnostic accuracy and efficiency, improved collaboration, and greater accessibility of pathology services. They also discuss various challenges that must be overcome. It also discusses the digital pathology ecosystem and the clinical and nonclinical applications of its use. Additionally, [21] highlights the barriers to the adoption of WSI, which include limitations in technology, image quality, difficulties in scanning all materials, slide storage, costs, the inability to handle high-throughput routine work, regulatory barriers, ergonomic concerns, and pathologists' reluctance.

Our contributions include:

- Highlighting the top three most-used methods for the acquisition, analysis, and storage of whole slide images. This breadth of coverage allows readers to gain a comprehensive understanding of the field.

- A comparative study of various methodologies used for different applications, along with their results and limitations, highlights the diverse applications and architectures of CNNs. This study provides valuable insights into the role of this technology in pathology research and practice.

## 2 REVIEW METHODOLOGY

We used the PRISMA methodology to screen articles. The articles written in English were reviewed. Standard databases such as Google Scholar, PubMed, Scopus, Crossref, and Web of Science were used to search for articles. The keywords used were "digital pathology," "AI and digital pathology," "whole slide imaging," and "deep learning."

All published articles were prescreened, removing commentaries, letters to editors, animal research, and case reports. Out of 381 articles, 20 were chosen. The prism diagram is described in Figure 3.

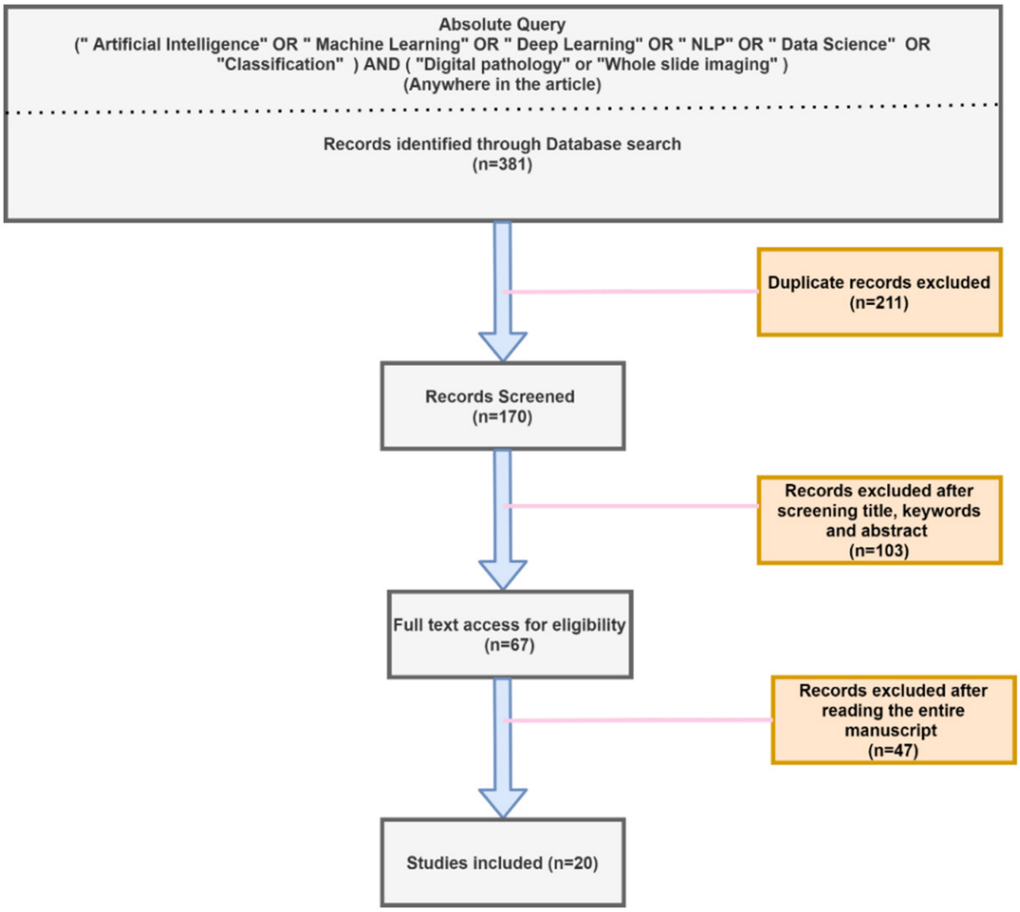


**Fig. 3.** PRISMA diagram

## 3 WHOLE SLIDE IMAGING: ACQUISITION, ANALYSIS, AND STORAGE

A whole-slide scanner is essentially a microscope controlled by robotics and computers. This is attached to a highly specialized camera containing advanced optical sensors. The entire setup includes a microscope, a light source, robotics for loading and moving glass slides, a computer, and software for processing, analyzing, storing, and viewing digital slides. The slides, including tissue microarrays [22], can be loaded into trays, racks, or carousels. The process of acquisition begins by loading the slide feeder with glass slides. WSI instruments are capable of batch scanning, where one slide is scanned at a time, and continuous or random-access processing, where slides can be uploaded while another is being scanned. Various vendors provide slide scanners with different batch capacities and compatibility. Scanning of slides can be done via two methods: tile-based and line-based [13]. Tile-based scanning employs a robotics-controlled motorized slide stage to scan various sections in the form of tiles [23], whereas line-based scanning utilizes a servomotor-based slide stage that moves in a jitter-free linear fashion to scan along a single axis [13]. Though tile-based scanning seems to be a more accurate scanning method, it focuses on the smallest sections of the specimen. However, the software must have the capability to handle this complexity. Otherwise, alignment issues at each point can lead to an increased number of artifacts. Line-based scanning is a relatively simpler process due to its methodology. The outputs consist of strips of images that are stitched together to form a complete image. The improved version of these techniques is TDI (time, delay, and integration) line scanning, which utilizes multiple line scan stages to enable faster imaging speeds and area scanning techniques [24, 25]. Two primary types of luminescence required for specimen acquisition are bright-field, traditionally utilizing tungsten lamps, and fluorescent scanning techniques, traditionally employing xenon arc lamps, mercury vapor lamps, and lasers [25]. These scanning cameras need to transfer the data captured from the sensors to the image processing unit, and this is accomplished with the assistance of a camera bus. We also see a mobile phone microscope used for acquiring WSIs [26].

Image analysis has gained popularity after the advent of digital imaging techniques and their transfer capabilities. The images produced as output are very large files that cannot be analyzed with basic tools. Hence, numerous new tools, such as video cameras, digital slide scanners, and WSI models, have captured the market. Several new software applications, such as TMarker, Orbit, and Qupath, with the primary goal of WSI analysis, have been developed [27]. For the analysis of WSI, one of the major requirements is the detection and classification of the nucleus in a cell. TMarker software uses a super pixel-based approach to classify nuclei as benign or malignant, and stained or unstained [28]. According to the results, it was found to be 76% accurate. As an application, it was used for cell counting and staining estimation of pathological IHC-stained tissue images with the assistance of techniques such as color deconvolution, super pixels, and active learning. Though it has proven to be accurate, it needs further validation and improvement on larger and more diverse datasets. Orbit is a tool for whole-slide image analysis that utilizes machine learning to comprehend the context within extensive WSI and applies this knowledge to analyze structures at various magnification levels. It utilizes a context-based structural classification method that can calculate various features across multiple image resolutions by processing the images in a tile-based manner. Orbit supports a variety of quantification methods, such as pixel classification and object segmentation. These methods lead us to the region of interest (ROI). Orbit is a user-friendly tool that can integrate with various algorithms in a straightforward manner [29]. Traditional bioinformatics methods heavily rely on prior knowledge and handcrafted features, which limits their capacity to uncover novel insights hidden within complex genomic data. On the contrary, unsupervised machine learning models offer the flexibility to learn intricate patterns without requiring labeled training data [30]. QuPath is an open-source digital pathology image analysis software that offers robust batch-processing and scripting capabilities, as well as a wide range of tools for tumor identification and high-throughput biomarker evaluation. It allows the creation of custom workflows and links them together with scripting functionality and existing software such as MATLAB and ImageJ. The development applications are Java 8 and JavaFX [31]. Histo-Cloud is a tool for pathologists that offers image segmentation functionality and allows for the extraction of features through a graphical user interface [32]. One of the major advantages of this tool is its ability to perform segmentation without staining the sample. The concept behind this, i.e., state-of-the-art CNN, is explicitly demonstrated by the segmentation of various structures from kidney tissues (renal histopathology).

After scanning the histology data with WSI scanners, it needs to be stored for future use. This is achieved with the help of the digital slide archive, which allows the physician to manage large collections of histologic images and integrate them with clinical and genomic metadata [33]. It allows you to view, search, and manage the data uploaded to the cloud remotely, i.e., without the need to download it to the device. It was a collaboration with HistomicsTK and Kitware, primarily focusing on managing cancer slides. A study at Emory University highlighted the importance of managing and querying both WSI and analytical results generated from images [34]. It, therefore, developed a database called the pathology image database system, which is a standard image-oriented database compatible with DICOM. This system was capable of storing images, making annotations, and retrieving them through a unified interface and architecture. Additionally, it can be integrated with PACS (picture archiving and communication system). An enhanced version of the storage system facilitates scalable storage of WSIs and rapid retrieval of image tiles by leveraging Apache Spark, a space-filling curve, and common data storage formats [35]. This study proposes two different methods of storing the WSI: parquet and ORC (optimized row columnar). ORC proved to be better in terms of fast retrieval and space efficiency for storage. Some additional storage image management software includes Slide Manager and Virtuoso, which can be utilized for storing, retrieving, viewing, annotating, and analyzing images [15]. Table 2 presents a summary of the techniques utilized for the acquisition, analysis, and storage of all slide images.

**Table 2.** Summary of the techniques used in WSI

| Author | Technique | Result | Novelty | Limitation |
|---|---|---|---|---|
| R. Hoffman et al. [23] | Tile Based Scanning | Classifying Biological Regions in Whole-Slide Histopathological Images | Using Tile-based technology in histopathology images | Complexity |
| N. Farahani et al. [13] | Line Based Scanning | Stripes of Images that needed to be stitched together | Slide navigation technique | loss of minute details as compared to tile-based |
| Patel et al. [24] | TDI line scanning | Multiple line scan stages to allow faster imaging | Multiple line scan stages | |
| Wild et al. [28] | TMarker for WSI analysis | Classification of nuclei that are benign or malignant and stained or unstained using a super pixeled-based approach. | Super pixeled-based approach | Validation is lacking for larger and different dataset |

*(Continued)*

**Table 2.** Summary of the techniques used in WSI *(Continued)*

| Author | Technique | Result | Novelty | Limitation |
|---|---|---|---|---|
| Manuel Strittl et al. [29] | Orbit for WSI analysis | Use of context-based structure classification for WSI image pixel classification, object segmentation, and object classification. | A user-friendly approach to compute various features at multiple magnification levels | |
| Peter Bankhead et al. [31] | Qupath for WSI analysis | Image analysis software using Java8 and JavaFX that provides a powerful batch-processing and scripting functionality | Open-source desktop software application that incorporates extensive annotation and visualization tools. Novel algorithm to create custom workflows. | |
| Brendon Lutnick et al. [32] | Histo-cloud for WSI analysis | Segmentation of different renal and non-renal WSIs and scalability demonstration. | Cloud-based tool. Developed easy-to-use plugins using Digital Slide Archive. | Limited applicability Needs the user to know the basics |
| David A. Gutman et al. [33] | Digital Slide Archive-built on a data management toolkit called Girder that is developed and maintained by Kitware | A cloud-based server for cancer investigators with a free digital pathology platform, avoiding the need for costly commercial software that is expensive to scale. | Remotely viewing, searching, and managing the data uploaded to the cloud | |
| Fusheng Wang et al. [34] | Pathology Image Database System | A database capable of storing images as well as annotations, retrieving through a unified interface and architecture. | Standard image-oriented database compatible with DICOM | Fast retrieval |
| Rao et al. [35] | Optimized Row Columnar | Scalable storage of WSIs and fast retrieval of image tiles. ORC type of storage was found to be better | Two different methods of storing the WSI, Parquet and ORC | |

## 4 USE OF ARTIFICIAL INTELLIGENCE IN DIFFERENT APPLICATIONS OF WHOLE SLIDE IMAGES

Using automated systems, such as artificial intelligence, for the classification and segmentation of whole slide images has recently gained prominence in the pathology research community. These systems are more efficient, accurate, and time-saving. Yottixel is an image search engine for extensive archives of histopathology whole-slide images and presents them in a compact format. The mosaic, i.e., patches of WSI, are converted into barcodes. The performance of the prototype platform is qualitatively tested using 300 WSIs from the University of Pittsburgh Medical Center and 202 WSIs from the Cancer Genome Atlas program provided by the National Cancer Institute. It uses various supervised and unsupervised algorithms, such as segmentation and clustering algorithms [36]. For any application of WSI using artificial intelligence, a sufficient quantity and quality of well-annotated data are required for training the model. Ink marking on the slides was deemed unsuitable; therefore, Jun Jiang *et al.* developed a system that digitally scanned the slides with annotations and then removed the annotations [37]. Recent studies mention that artificial intelligence (AI) is playing a significant role in cancer detection. For instance, a deep learning cluster can be beneficial for illustrating the immunophenotypes and functional heterogeneity of the tumor microenvironment in patients with bladder cancer (BLCA) [38]. Further, if the AI score is calculated, it can quantify the clusters within the WSI. AI-based algorithms have proven to be a valuable tool in detecting prostate adenocarcinoma and Gleason grading using multilayer CNNs specifically designed for image classification tasks [39]. The instrumentation requirement for acquiring the WSI in this case was determined to be a 40× magnification scanner (Philips Intellisite Scanner) with slide-level analysis. The algorithm is highly accurate, based on a large, blinded, external validation dataset, for identifying and quantifying prostate cancer. Along with classification tasks, some algorithms can be used for the localization of abnormal regions in WSI, making it easier for the pathologist to focus on the region of interest [40]. It was done for colorectal cancer using a customized Inception-ResNet-v2 Type 5 (IR-v2 Type 5) model. Diabetic retinopathy diagnosis typically involves the manual examination of retinal fundus images by ophthalmologists, which can be time-consuming and prone to human error. Automated DR diagnosis using AI and image processing techniques has the potential to improve diagnostic accuracy and efficiency [41].

Similarly, another model for cancer detection could be the residual neural network-18 (ResNet-18), an 18-layer deep CNN, and ResNet-50, a 50-layer deep CNN, to identify primary cutaneous squamous cell carcinoma with a risk for metastasis [42]. These ResNet module architectures were trained and then fine-tuned using a single tumor tile AI model. The technique used here is easy to implement and visualize but is prone to label noise. For any WSI analysis, the balance between specificity and selectivity is crucial for reducing false positive predictions. To address these issues with balance [43], it was suggested to implement two deep CNNs. The first network should prioritize higher sensitivity, while the second should prioritize higher specificity. The screening was conducted on digitized slides for mycobacteria using a patch-based approach. This algorithm also included an additional feature that presented the detected mycobacteria in a web-based gallery format alongside the WSI for the pathologist to review.

There are various models of AI techniques being utilized in histopathology diagnoses of WSI, as discussed and reviewed by the authors in their paper [44]. The CNN extracts features from the region of interest derived from the whole slide image to gather information for regression fitting tasks. Under CNN, the EfficientNet series models were found to have remarkable advantages over previously used models [45]. With the help of this, a chronic rhinosinusitis evaluation platform was built to obtain the proportion of inflammatory cells needed for cellular phenotyping and the diagnosis of nasal polyps.

Convolutional neural networks can also be used to distinguish between two different forms of pathological issues, for example, differentiating Spitz and conventional forms of melanocytic lesions [46]. The patches from the lesions were curated and then processed using CNN for classification. The major limitation of using CNN for this application is its accuracy, which was 92%. Nasopharyngeal carcinoma (NPC) is a type of head-and-neck cancer. To detect this cancer, 220 NPC patients were divided into training, internal, and external test cohorts. Radiomic features were extracted from MRI images selected and integrated into the radiomic signature. This histopathological signature was extracted from the WSI of biopsy specimens using an end-to-end deep learning method [47]. In neuropathology, deep learning approaches have been reported for classifying Alzheimer's disease pathophysiology in magnetic resonance and positron emission tomography images, as well as for correlating gene expression with the neuropathology dataset [48]. Previous studies have predominantly relied on CNNs for AD diagnosis using MRI data. However, these models often struggle to capture long-range dependencies due to their limited receptive fields. In contrast, swin transformers demonstrate superiority in handling hierarchical representations, making them suitable candidates for AD detection tasks [49]. The swin transformer architecture is used to generate segmentation masks of different brain structures. The model employs self-attention mechanisms to capture contextual information at varying scales, thereby overcoming limitations associated with conventional CNNs. Secondly, traditional human image detection methods often rely on deep learning models that require large amounts of annotated data for training. However, these models may struggle with detecting humans in complex backgrounds or under occlusions [50]. Al-Hazaimeh proposed a geometric-based approach and evaluated it on standard human detection benchmarks, including datasets with varying levels of complexity and occlusions. The results demonstrated improved detection accuracy and robustness compared to traditional deep learning-based methods, especially in challenging scenarios.

Table 3 presents a summary of AI in various applications of WSI.

**Table 3.** Summary of different applications of WSI using AI

| Ref | Application | Methodology | Result | Novelty | Limitation |
|---|---|---|---|---|---|
| Shivam Kalra et al. [36] | Image Search Engine | CNN<br>The patches of WSI are converted to Barcodes | Except for the rectum adenocarcinoma, all other graphs show that hit rate values reach ~ 100%<br>As for the classification task, the recall and sensitivity are-<br>Adrenal gland (0.90,0.91), Brain (0.87,0.87), Kidney (0.70,0.68), colorectal (0.52,0.59), uterus (0.55,0.96) and lung (0.70,0.70) | Supervised and unsupervised algorithms, including segmentation and clustering algorithms for search application | Accuracy and speed, which can be improved further |
| Jun Jiang et al. [37] | Annotation removal | Conditional generative adversarial network (GAN) based on Pix2Pix. | With this method, a decrease in image fidelity after cleaning was observed.<br>For the tissue-only patches, both PSNR and SSIM slightly increased, but VIF changed only slightly. | Concept that allows us to annotate the training data without ink marks affecting the analysis | Relative blurriness of some colour-normalized images<br>Computational time |
| Yiheng Jiang et al. [38] | Bladder Cancer | k-means Cluster formation with deep learning and CNN | The average classification accuracy came out to be 86%, and the AUC was found to be 0.95 | Use of Deep learning modules in the field of BLCA | – |
| Liron Pantanowitz MD et al. [39] | Prostate Cancer diagnosis in WSI of core needle biopsies | Multilayer Convolutional Neural Network | AUC of 0.997 for the internal test and AUC of 0.991 for the external test | High-performance characteristics of a multifunction algorithm by extending its study beyond just detection and grading, which is one of the first models to be used as clinical validation as a routine pathology practice. | Ground truth is sometimes difficult to reach.<br>The algorithm is generalized and, therefore, needs experts. |

*(Continued)*

**Table 3.** Summary of different applications of WSI using AI *(Continued)*

| Ref | Application | Methodology | Result | Novelty | Limitation |
|---|---|---|---|---|---|
| Pushpanjali Gupta et al. [40] | Colorectal cancer | CNN<br>Customised Inception-ResNet-v2 Type 5 | For the pre-trained CNN, the sensitivity of VGG16 was found to be the highest, i.e., 0.99 ± 0.012 and an AUC of 0.96.<br>For the custom model, the AUC was reduced except for Customized Inception-ResNet-v2. Among Inception-ResNet-v2 variants, type 5 obtained an AUC of 0.99 | Customizing the pre-trained model to increase the accuracy in the detection of colorectal cancer | Population considered in this study representing only a specific region.<br>The slides used for collecting the WSI belonged to a single hospital, reducing generality. |
| Jaakko S. Knuutila et al. [42] | Detection of primary cutaneous squamous cell carcinoma | CNN (ResNet 18 and ResNet 50 architecture) | In the single-tile model, the AUROC obtained was 0.689.<br>With Rapid metastasis, the AI model was 0.814 with an accuracy of 73% | | Prone to label noise<br>Overfitting |
| Liron Pantanowitz et al. [43] | Mycobacteria | Two CNN (GhostNet)<br>Patch-based deep learning approach | The algorithm showed an AUC of 0.96, a sensitivity of 0.60, and a specificity of 0.99 at the image patch level, while an AUC of 0.9, a sensitivity of 0.83, and a specificity of 0.80 at the WSI level. | Two Deep Convolutional Neural Networks to achieve a balance between sensitivity and specificity | Clinical validation |
| Qingwu Wu et al. [45] | Cellular phenotyping diagnosis of nasal polyps by WSI based on the proportions of inflammatory cells | CNN (efficient net) | AICEP 2.0 could quantify all four types of inflammatory cells as compared to only eosinophils in AICEP1.0. The MAE% and PMSE% difference between them was approx. 5%. | This methodology was first to confirm the positive correlation between the percentage of peripheral blood eosinophils and eosinophils in polyp tissue on WSI, and it could predict whether patients were eCRSwNP or not. | The real-world diagnostic accuracy of AI was lower. |
| Steven N. Hart et al. [46] | Melanocytic lesions | CNN | For the curated patches, both de novo and pre-trained networks had a validation accuracy of 99.0% and 95.4%, respectively.<br>For noncurated patches, it was 52.3%. | Obtaining the result with the help of | The training took significantly longer and had lower overall performance. |
| Fan Zhang et al. [47] | Nasopharyngeal Carcinoma | DCNN (Resnet-18) multi-scale nomogram | Multi-scale nomogram showed a consistently significant improvement in predicting treatment failure compared with the clinical model in the training with a C-index of 0.817 versus 0.730, $p < 0.050$. | It utilised a computer-aided algorithm to predict treatment failure. | Retrospective nature and relatively small sample size of data.<br>A molecular profile was not included in the multi-scale model.<br>The validation study was done on subjects that were all Chinese cohorts. |

## 5 DISCUSSION

Advancements in deep learning models, particularly in the fields of image analysis and pattern recognition, show great promise for improving the accuracy and effectiveness of digital pathology systems. These improvements will contribute to more accurate and prompt diagnostic outcomes, thereby positively impacting patient care. With the increasing sophistication and reliability of AI algorithms, their integration into routine clinical practices is becoming inevitable. Digital pathology applications may involve supporting pathologists in making diagnoses, prioritizing cases, and forecasting patient prognosis by analyzing histopathological images.

The expansion of digital pathology for telepathology and remote consultations is anticipated due to its ability to facilitate global cooperation among pathologists, bridge geographic barriers, and promote equitable access to specialized pathology services, especially in underprivileged regions. By integrating digital pathology data with other "omics" information, such as genomics and proteomics, researchers can gain deeper insights into disease processes and develop novel therapeutic strategies.

To ensure seamless integration with other health IT systems and promote data sharing and collaboration, ongoing efforts are being made to standardize and improve the interoperability of digital pathology platforms. Such initiatives aim to streamline workflows, foster innovation, and accelerate progress in personalized medicine and biomedical research. Digital pathology faces several challenges due to the lack of standardized infrastructure, hindering the seamless exchange of data and images. The substantial data volumes generated, with biopsy slides often requiring several gigabytes per patient, present storage challenges, especially for facilities in resource-constrained countries. Ensuring interoperability among different digital pathology systems is a key challenge that impacts data retrieval, navigation, and integration with other healthcare IT systems. Compliance with existing regulations and the development of frameworks for new ones are vital for the successful implementation of digital pathology systems, requiring careful management of regulatory and compliance issues. Moreover, establishing specialized training programs and resources is crucial to ensuring the correct usage and interpretation of digital images. However, this can be challenging due to the diverse workflows and technologies employed in different laboratories.

One potential area for future research in digital pathology is investigating the tumor microenvironment through AI-powered techniques. The tumor microenvironment is a complex ecosystem consisting of various cell types, such as CD8 T cells, NK cells, regulatory T cells, apoptotic cells, dendritic cells, and myeloid cells. The presence and distribution of these cell types within tissues can provide valuable insights into diseases and the mechanisms of action of drugs. Human pathologists often find it challenging and time-consuming to identify relationships between cell types and tissue regions. However, with the use of WSI and AI interpretations, this process can be streamlined. AI-powered digital pathology can provide metrics related to cell counts, densities, and spatial relationships across various cell types and tissue regions. This approach has the potential to revolutionize our understanding of the tumor microenvironment and its role in disease progression and treatment response.

Artificial intelligence image management systems have the potential to revolutionize pathology by enabling pathologists to identify cells with greater confidence and accuracy. These systems utilize algorithmic scoring mechanisms to analyze pathology images, offering quantitative metrics that can assist in diagnosis and treatment planning. By leveraging AI, pathologists can benefit from improved workflow efficiency and more accurate diagnostic outcomes.

Adding on to that, considering the large size of pathology datasets and the significant storage requirements they entail, integrated workflow solutions are becoming increasingly important. LIS systems that are integrated with WSI and EMR systems enable physicians to access annotated images of pathologic slides along with their interpretations at the point of care. This integration streamlines the diagnostic process, enhances collaboration between pathologists and clinicians, and improves patient care outcomes.

In summary, the adoption of AI image management systems and integrated workflow solutions represents a promising future direction for digital pathology. It offers opportunities to enhance diagnostic accuracy, improve workflow efficiency, and facilitate better patient care.

## 6 CONCLUSION

This comprehensive review highlights the significant advancements in digital pathology, with a specific focus on WSI. The paper emphasizes how WSI has revolutionized the acquisition, analysis, and storage of pathology images, presenting a digital alternative to traditional microscopy. These advancements have been largely driven by the integration of deep learning modules, particularly CNNs, into digital pathology workflows.

Conventual neural networks have emerged as highly effective tools for various tasks in digital pathology, such as image analysis, classification, distinguishing between different tissue types, and retrieving relevant information from large datasets. Their ability to learn complex patterns and features from pathology images has made AI models the cornerstone of many digital pathology applications, leading to their widespread adoption in the field. Despite the considerable progress made in digital pathology, achieving full automation of the system remains a significant research challenge. One of the key obstacles is the high pixel density of whole slide images, which increases storage requirements and poses challenges for data management and processing. Additionally, issues related to standardizing slide navigation and ensuring interoperability between different digital pathology systems need to be addressed to facilitate seamless integration and data sharing.

To overcome these challenges, researchers are exploring various solutions, such as implementing cost-effective components like stepper motors to facilitate easy slide navigation. The paper acknowledges the challenges that remain in achieving full automation of the digital pathology system. By identifying obstacles such as the high pixel density of whole slide images and issues related to standardization and interoperability, the paper demonstrates a clear understanding of the current limitations in the field. These efforts aim to enhance automation, standardization, and interoperability in digital pathology, ultimately resulting in more efficient and accurate pathology workflows.

In conclusion, the field of digital pathology continues to advance rapidly, driven by ongoing research efforts to overcome existing limitations. Future research should focus on further improving automation, standardization, and interoperability to realize the full potential of digital pathology in enhancing patient care and outcomes.

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