



## Review Article

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# The imperative of integrating digital image analysis in evaluation of tumor tissue: A Review of African Contemporary Landscape

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## Abstract

Digital Image Analysis (DIA) has emerged as a transformative technology in the evaluation of tumor tissue. This offers significant improvements in accuracy, reproducibility, and efficiency of diagnosis. Traditional histopathological methods rely on manual interpretation and often suffer from variability and subjectivity with limited turnaround time. Leveraging advanced algorithms and machine learning (ML) techniques provides objective and standardized assessments that enhance diagnostic precision and consistency. Technological advancements, particularly the development of Whole Slide Imaging (WSI) and sophisticated WSI scanners, have been pivotal in advancing DIA. These tools facilitate the acquisition of high-resolution, detailed images of the entire tissue sections, enabling comprehensive analysis. The integration of powerful software tools and AI algorithms further enhances the diagnostic process by automating routine tasks and providing precise quantitative analyses of histopathology and cytopathology. Machine learning, specifically deep learning, plays a crucial role in DIA. Deep learning models, trained on vast datasets of histopathological images, can identify complex patterns and correlations, aiding in detecting and classifying tumors. These AI-driven tools offer the potential for real-time analysis and predictive modeling, significantly impacting clinical decision-making and personalized patient care. Despite its numerous advantages, DIA faces challenges including technical issues related to image quality and data management, as well as the need for rigorous validation and standardization of algorithms. Additionally, the cost and accessibility of DIA technology pose barriers to its widespread adoption, particularly in resource-limited settings. The future of DIA is promising, with ongoing advancements in imaging technologies, multi-omics integration, and AI. These developments are expected to enhance the capabilities of DIA further, making it a standard practice in pathology and improving patient outcomes. As DIA continues to evolve, it holds the potential to revolutionize the histochemical evaluation of tumor tissue, offering new opportunities for innovation in diagnostics and personalized medicine in the African landscape.

**Keywords:** Integrating; digital; image; analysis

## Background

Evaluation of tumor (new growth) tissue involves the examination of tissue samples using various techniques to identify cellular and molecular features characteristic of the cancer

environment. Traditional methods rely heavily on the expertise of pathologists to visually inspect and interpret stained (mostly hematoxylin and eosin) tissue sections under a microscope,

which can be subjective and variable [1,2]. Accurate and efficient tumor tissue environs analysis is critical for the correct diagnosis, prognosis, and treatment planning for cancer patients. Traditional methods, while effective, often suffer from limitations such as inter-observer variability, labor-intensive processes, and reduced turnaround time [3]. The conventional method of histochemical evaluation of tissue relies on the pathologist to look out for features that are made possible to identify after the tissue sections have been treated with histochemical stains or reagents, such as Immunohistochemistry, Haematoxylin, and Eosin (H&E), and other histochemical stains to highlight cellular components for visual interpretation by pathologists [4,5,6].

A tumor tissue is an abnormal mass of tissue formed when cells grow and divide at rates that are faster than normal, or when cells apoptotic signals when they should. Some tumors are benign, meaning that they are not an indication of cancer and don't spread into surrounding parts of the body. Benign tumors tend to stay in one spot on a person's body, instead of invading neighboring regions. They typically grow slowly and have distinct borders. Other tumors are cancerous or malignant and do invade other areas of the body via the bloodstream and lymphatic systems and seeding. Benign tumors have the potential to eventually turn into malignant tumors and require close monitoring by the patient and their healthcare provider [7, 8]. Telepathology is the practice of pathology at a distance. It uses telecommunications technology to facilitate the transfer of image-rich pathology data between distant locations for diagnosis, education, and research [9,10]. Telepathology enables the transmission of digital pathology images for primary diagnosis, quality assurance, education, research, or second-opinion diagnoses. Though barriers to implementation exist, there are potential benefits, such as the wide spectrum of uses like frozen section, primary diagnosis, and second opinions.

Telepathology represents an innovation that may transform the future of pathology practice [11]. The performance of telepathology requires that a pathologist selects the video images for analysis and the rendering for diagnoses [12]. Whole Slide Images (WSI) are high-quality images of slides taken using high-resolution cameras or slide scanners. These images are then augmented and serve as digital images of the slide which can be stored and shared for remote review by a distance pathologist. Conventionally, histochemical image analysis at the level of light microscopy proves tedious and with marked observer variability. The advent of digital pathology (Telepathology) brought about the Whole Slide Imaging (WSI) technique in histopathology and has revolutionized histopathology image analysis from a 'pathologist-to-microscope' review to a 'peer review' or 'remote review' using WSI techniques.

Digital Image Analysis (DIA) came to the forefront stemming from advances in technology and research. It employs digital tools in the analysis of histopathological features for diagnoses. This is achieved by employing advanced programming tools, data gathering, machine learning (ML), and Deep Learning (DL), to develop a digital model that is trained to identify features in a WSI [4,6,7]. With the widespread adoption of digital slide scanners in both clinical and preclinical settings, it is becoming increasingly

common to digitize histology slides into high-resolution images. Machine learning can be utilized for various image analysis tasks that are routinely performed during histological analyses including detection, segmentation, and classification. These tools have greatly reduced the laborious and tedious manual work in image analysis and can reduce inter-observer variability in reaching diagnostic consensus [13]. Machine Learning focuses on methods to construct computer programs that learn from data concerning some class of tasks and a performance measure, has been widely applied in several challenging problems in bioinformatics due to the algorithm's ability to extract complex relationships from high-dimensional data.

Conventional machine learning methods (e.g., random forest, support vector machines) are limited by their ability to extract features from raw data. Efforts have been invested in careful feature engineering and domain knowledge to construct informative features to train the model though certain engineered features are difficult to interpret biologically and have limited utility in biomedical applications. In early 2000, several breakthroughs in deep learning, the availability of large datasets, and advancements in computing power have reenergized machine learning and applications in real-world problems [14]. Deep learning (DL) is a family of new machine learning models composed of multiple processing layers that learn representations of data with multiple levels of abstraction without feature engineering. These methods have dramatically improved the state-of-the-art in multiple domains ranging from speech and text recognition to object detection in biomedical applications [15-19]. Advances in DIA have seen the emergence of the various models and tools that are employed in histochemical image analysis. These tools have proven to be reliable as they present with accuracy, efficiency, and reproducibility in tumor diagnosis [5]. It has been employed in the diagnosis of breast cancer, lung cancer, and colon cancer. A recent study proposed a novel AI system for colorectal cancer (CRC) diagnosis based on transferred-learned deep convolutional neural networks. This system consistently agreed with expert pathologists and achieved better performance in diagnosing CRC whole-slide images (WSIs). It alleviates the clinical burden and improves treatment for CRC patients [20].

The field of cancer pathology has proven to be supremely suitable for the development of machine learning models, in no small part due to the construction of publicly available, curated whole slide image (WSI) datasets from initiatives like the Cancer Genome Atlas (TCGA), Clinical Proteomic Tumor Analysis Consortium (CPTAC), and the Cancer Image Archive (TCIA) [21,22]. The datasets contained within these repositories often include other related data, such as clinical characteristics, patient outcomes, molecular analyses, and other imaging modalities, in addition to the WSIs. These data can be utilized as target features, such as predicted progression-free survival duration, or even integrated into the machine learning model for higher dimensional analysis. The numerous types of cancer collected by these repositories allow researchers to focus their applications as narrowly or broadly as they desire, from single subtypes (e.g., lung adenocarcinoma) to

pan-cancer analyses. The majority of machine learning applications in this field rely on supervised learning methods based on clinical parameters or pathologists' annotations to generate training datasets. Within supervised learning approaches, there exist several distinct resolutions of annotation required to generate a high-quality training dataset depending on the scale of the analysis. The ultimate goal of machine learning applications for histopathology is to generate clinically beneficial output, but this may be achieved in a wide variety of ways. Model designed to flag regions of concern for a pathologist to review in detail and a tool that identifies cancer patients that are likely to respond to immunotherapies by classification of immune cell types are likely to improve clinical outcomes, but these two models will require very different training datasets. Three different scales of histopathological analyses that machine learning can operate within WSI-level, region of interest (ROI)-level, and cell-level [23] are considered. This review aims to explore the advances in digital image analysis and its role in enhancing the histochemical evaluation of tumor tissue, highlighting technological developments, applications, and prospects.

## Historical Perspective and Advances in Digital Image Analysis

Traditional histochemical techniques like hematoxylin and eosin (H&E) staining, immunohistochemistry (IHC), and in situ hybridization (ISH) methods have been the cornerstone of pathology for decades, providing vital information on tumor morphology and molecular markers [1]. Despite their utility, conventional methods have limitations such as subjective interpretation, variability among pathologists, and time-consuming processes. These challenges have led to diagnostic inconsistencies and delays in patient management [3]. The advent of digital pathology has revolutionized the field of histochemical evaluation using whole-slide imaging. Whole slide imaging (WSI) allows for the digitization of entire tissue slides, enabling detailed analysis and sharing of images. The integration of high-resolution imaging and computational power has facilitated the development of robust image analysis algorithms [24,25].

Whole Slide Imaging (WSI) represents a significant technological leap in digital pathology. WSI involves the scanning of entire glass slides at high resolution to produce detailed digital images that can be viewed and analyzed on a computer screen. This technology allows for the comprehensive digital capture of histological slides, facilitating remote access, sharing, and analysis of tissue samples. The generation of whole-slide images (WSI) relies on advanced imaging technologies and sophisticated hardware and software to digitize histopathological slides [26]. Whole-slide scanners are specialized devices designed to digitize entire tissue sections on glass slides. Key components and functionalities of these scanners include High-Resolution Cameras that capture detailed images of tissue sections at various magnifications, motorized Stages that move the slide to capture the entire tissue section in a series of high-resolution tiles and optical Systems: High-quality lenses and optics to ensure clarity and detail in the captured images. Several

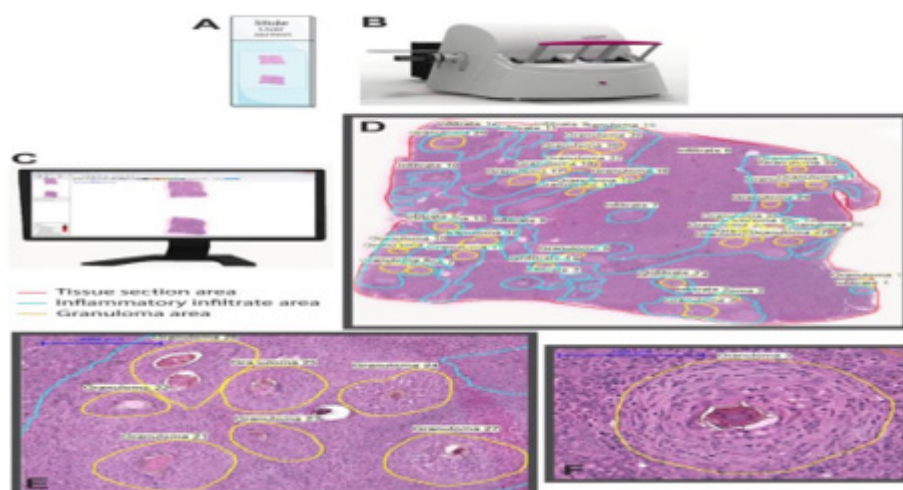
advanced WSI scanners are available on the market, each offering unique features and capabilities. These scanners are designed to handle high-throughput scanning, ensuring both speed and accuracy. Popular WSI scanners include the Aperio AT2 (Leica Biosystems), Panoramic 250 (3DHISTECH), and Ventana DP 200 (Roche).

## Image Management Systems in WSI

Once digitized, whole-slide images are stored and managed using image management systems (IMS). These systems provide tools for storage and retrieval allowing large WSI files and retrieved quickly for analysis; Annotation and Analysis allow pathologists to annotate regions of interest and perform quantitative analysis. Sharing and collaboration enable remote access and sharing of WSI for telepathology and collaborative research. Developing a Whole slide image involves the following steps- Slide Preparation: Tissue samples are collected, processed, and stained using standard histopathological techniques. These slides are then prepared for scanning by placing them on the scanner's motorized stage. Scanning: The whole-slide scanner captures the tissue section by moving the slide in a coordinated manner under a high-resolution camera. The scanner captures multiple overlapping image tiles at high magnification. Image Stitching Software: The digitization process involves capturing multiple image tiles, which are then stitched together to form a complete whole-slide image. Advanced software algorithms align and merge these tiles seamlessly to produce a single, high-resolution image [26,27]. Quality Control: The digitized whole-slide image undergoes quality control to ensure clarity and accuracy. Any artifacts or errors introduced during scanning are identified and corrected (Figure 1.1).

## Digital Image Software and Tools

Numerous software and tools have been developed to assist in digital image analysis. Platforms like ImageJ, QuPath, and Aperio provide functionalities for image processing, annotation, and quantitative analysis. These tools have been instrumental in enhancing the precision and reproducibility of histochemical evaluations [29]. Digital pathology, which is the process of digitizing histopathology images, creates a new "treasure trove of image data" for machine learning (ML) and deep Learning (DL) [23]. Machine learning and deep Learning can be utilized for various image analysis tasks that are routinely performed during histological analyses including detection, segmentation, and classification. Some commercial image analysis software already incorporates machine learning algorithms to assist researchers and clinicians in quantifying and segmenting histopathological images. These tools have greatly reduced the laborious and tedious manual work in image analysis and can reduce inter-observer variability in reaching diagnostic consensus [13,23]. Digital pathology relies on sophisticated software tools that enable the analysis and interpretation of WSI images. These tools provide functionalities for image processing, annotation, and quantitative analysis, enhancing the accuracy and efficiency of histochemical evaluations [29,30,31].



**Figure 1.1:** Whole slide imaging of a liver section showing granulomas elicited by *Schistosoma mansoni* infection in mice. After loading the slides (A) in the scanner (B), a built-in digital camera captures the entire tissue section and viewer software generates a high-resolution digital slide (C), which can be assessed by the operator by selecting and marking the area (s) of interest for qualitative and quantitative analyses. In (D), a representative digital slide in which granulomas and non-granulomatous inflammatory regions were manually outlined for subsequent morphometric evaluations using associated software. In (E, F), granulomas are seen at high magnification. The equipment and software illustrated in this figure are the 3D Histech Panoramic scanner and Panoramic Viewer 1.15.2 SP2 RTM software, respectively [28].

## Key Software Tools in Digital Pathology

ImageJ is an open-source image processing program designed for scientific multidimensional images. It provides a wide range of plugins for image analysis, including segmentation, measurement, and enhancement. QuPath is another open-source software platform specifically developed for digital pathology. It offers powerful tools for slide viewing, annotation, and machine learning-based analysis, making it suitable for both research and clinical applications [30]. Aperio Image Scope is yet another commercial software by Leica Biosystems that allows for the visualization and analysis of digital slides. It includes tools for image annotation, measurement, and algorithm-based analysis. Comprehensive image analysis software that provides advanced tools for tissue segmentation, biomarker quantification, and machine learning integration can be achieved using Visiopharm software [32,33].

## How Digital Image Software and Tools Work

Image Processing is first achieved by software tools preprocessing the scanned images to enhance contrast, remove artifacts, and adjust color balance. This step ensures that the images are suitable for detailed analysis. This is followed by segmentation, the software segments the tissue into different regions of interest (e.g., tumor vs. non-tumor areas) using algorithms that identify specific histological features. Annotation is the third step where the Pathologists and researchers can annotate images to highlight areas of interest, such as regions of high cellularity or areas with specific staining patterns. Finally quantitative Analysis using advanced algorithms measuring parameters, such as cell density,

nuclear size, and staining intensity. These quantitative metrics provide objective data that can be used for diagnostic and research purposes. Machine Learning Integration: Some software platforms incorporate machine learning models that can be trained on annotated datasets to automatically classify tissue types, detect abnormalities, and predict clinical outcomes [32,33].

## Machine Learning and Deep Learning in Digital Imaging

Machine learning (ML) and deep learning (DL) are integral components of digital image analysis (DIA) in histopathology and have significantly contributed to advancements in digital pathology. Algorithms can be trained to recognize patterns and classify tissue samples with high accuracy. Deep learning models, in particular, have shown promise in identifying complex histopathological features and predicting clinical outcomes [34]. These technologies automate the recognition and analysis of histological features, enhancing the precision, reproducibility, and efficiency of cancer diagnosis and research. Convolutional Neural Networks (CNNs) excel at recognizing complex histopathological patterns, detecting mitotic figures, and classifying tumor types with remarkable accuracy [5,6]. Machine learning (ML) and deep learning (DL) are subsets of artificial intelligence (AI) that have significantly impacted digital image analysis in the histochemical evaluation of tumor tissue. These technologies facilitate automated, precise, and reproducible analysis of histopathological images, aiding pathologists in diagnosing and understanding tumor biology.



## Developing Machine Learning and Deep Learning Models for Digital Image Analysis

The following steps are procedures in developing Machine learning and deep learning models in digital image analysis.

### Data Collection and Annotation

The foundation of ML and DL models in DIA lies in a robust dataset of histopathological images. These images are typically obtained from digitized slides of stained tissue sections, which capture detailed histological features necessary for training AI models. High-quality annotated datasets are crucial. These datasets consist of digitized whole slide images (WSIs) with detailed annotations provided by expert pathologists, indicating areas of interest such as tumor regions, normal tissue, and specific histological features [33].

### Data Preprocessing

The collected images undergo preprocessing to enhance image quality and prepare them for analysis. This includes normalization, contrast adjustment, noise reduction, and artifact removal [31]. AI models, the images undergo several preprocessing steps: i. Normalization: Adjusting image intensity values to a common scale to ensure consistency across the dataset. ii- Augmentation: Generating additional images through transformations (e.g., rotations, flips, scaling) to increase dataset variability and robustness. iii. Segmentation: Identifying and isolating regions of interest (e.g., specific cells or tissue structures) within the images to focus the analysis on relevant features [35].

### Feature Extraction and Annotation

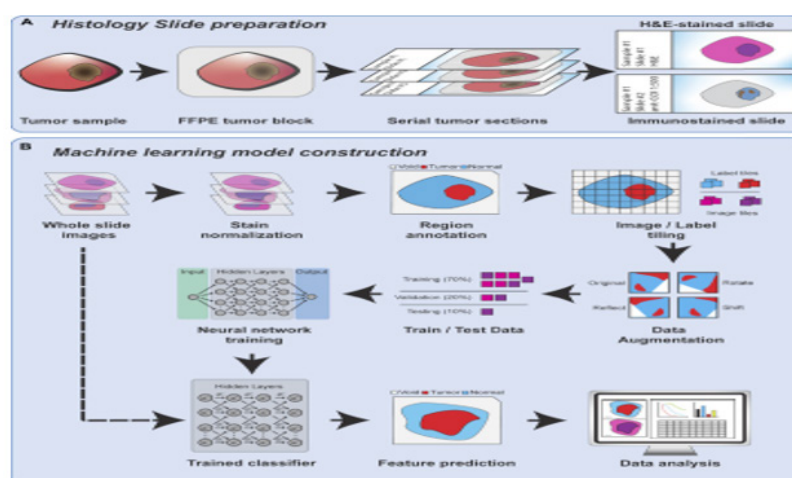
Traditional ML models often require manual feature extraction, where specific characteristics like texture, shape,

and color are identified. In DL, convolutional neural networks (CNNs) automatically extract features from raw image data through multiple layers of convolutional operations [32]. Expert pathologists annotate the images by labeling various histological features, such as cell types, structures, and abnormalities. These annotated images serve as the ground truth for training ML and DL models. Accurate and detailed annotations are crucial for the model to learn effectively. Model training learns associate the extracted features with specific labels (e.g., cancerous vs. non-cancerous tissues) by minimizing the error between predicted and actual labels through a process called back propagation. The preprocessed data is used to train the ML or DL model to reduce inaccuracies. In supervised learning, the model learns to associate input images with corresponding annotations or labels through optimization, minimizing the difference between predicted and actual labels [15]. Training a machine learning model for image segmentation requires a large amount of high-quality, labeled images as a training dataset. Therefore, building an effective training dataset requires a careful balancing of data quantity, data quality, and cost. In comparison to many other fields that utilize computer vision, the amount of publicly available histopathology data suitable for training a machine learning model is quite limited [23].

### Validation and Testing

Models are validated and tested using separate datasets to evaluate their performance. metrics such as accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC-ROC) are used to assess the model's predictive capabilities [36]. The percentage of correct predictions made by the model, the ratio of true positive predictions to the total predicted positives (precision). The ratio of true positive predictions to the total actual positives and F1-Score provide a balanced measure of the model's performance.

### Deployment and Inference



**Figure 1.2:** An overview of histology slide preparation and machine learning model construction process [23].

After successful validation, the model is deployed in clinical settings where it can analyze new histopathological images. The model's predictions assist pathologists in diagnosing and characterizing tumors more efficiently and accurately. The integration of DIA into clinical workflows lead to more consistent and objective evaluations, reducing variability between pathologists and improving diagnostic accuracy (Figure 1.2).

## Role of DIA in Tumor Tissue Evaluation

Digital Image Analysis (DIA) has revolutionized tumor tissue evaluation by enhancing accuracy, reproducibility, and efficiency. Its integration into pathology provides significant benefits across several dimensions, including quantitative analysis, diagnostic accuracy, and workflow efficiency.

### Accuracy and Reproducibility

One of the primary advantages of DIA in tumor tissue evaluation is its ability to provide consistent and accurate results. Traditional histopathological evaluation relies heavily on the subjective interpretation of pathologists, which can lead to variability in diagnoses. DIA reduces this variability by providing objective measures and standardized analysis. Studies have shown that DIA can improve inter-observer agreement and diagnostic consistency in assessing tumor characteristics [31,33], and AI-assisted analysis can match or exceed the performance of experienced pathologists [37]. DIA enables precise quantitative analysis of histological features, which is crucial for understanding tumor biology and progression. It allows for the measurement of various parameters such as cell density, nuclear size, and staining intensity, providing detailed insights into tumor morphology and heterogeneity. DIA can quantify the expression of biomarkers like HER2, Ki-67, and PD-L1, which are essential for prognosis and treatment planning in cancers such as breast and lung cancer [15,32]. Automated image analysis can measure the expression levels of proteins, nucleic acids, and other molecular markers, providing valuable insights into tumor biology [38]. The integration of DIA in pathology workflows significantly enhances speed and efficiency. Automated image analysis reduces the time required for slide review and interpretation, allowing pathologists to focus on complex cases and decision-making. Additionally, DIA facilitates high-throughput analysis, which is particularly beneficial in large-scale clinical studies and research [25]. Automated analysis reduces the time required for slide review and data interpretation, allowing pathologists to focus on complex cases and improve overall productivity [39].

Numerous clinical case studies have demonstrated the efficacy of digital image analysis in routine diagnostics. For instance, studies on breast cancer histopathology have shown that digital platforms provide reliable primary diagnoses, aiding in timely and accurate treatment decisions [38]. DIA is extensively used for biomarker analysis, providing quantitative data on protein expression and distribution. This is particularly important in personalized medicine, where biomarker levels guide therapeutic decisions [15]. DIA assists in the grading and staging of tumors by providing detailed morphological and molecular analyses, which

are essential for determining the aggressiveness and progression of cancer [32]. In research settings, DIA is invaluable for high-throughput screening of tissue samples, helping to identify novel therapeutic targets and understand drug responses [31]. Digital pathology is a powerful tool for research, enabling high-throughput analysis and the discovery of novel biomarkers. It supports large-scale studies by providing consistent and reproducible data, which is essential for validating research findings [15]. Also, comparative studies between digital and traditional methods have highlighted the advantages of digital pathology. For example, deep learning models have been used to predict lymph node metastasis in breast cancer, outperforming traditional manual methods in accuracy and efficiency [40].

## Challenges and Limitations

Despite the numerous advantages of Digital Image Analysis (DIA) in the histochemical evaluation of tumor tissue, several challenges and limitations need to be addressed to fully realize its potential in clinical practice.

### Technical Challenges

Despite its benefits, digital image analysis faces technical challenges such as image quality variability, data storage requirements, and the need for robust computational infrastructure. Ensuring the reliability and consistency of digital tools is crucial for their widespread adoption [41].

### Image Quality and Artifacts

High-quality digital images are essential for accurate analysis. Variability in staining, tissue preparation, and imaging conditions can introduce artifacts that affect the performance of DIA algorithms. For instance, variations in tissue thickness, staining intensity, and scanner calibration can lead to inconsistencies in analysis results [31].

### Data Management

The sheer volume of data generated by Whole Slide Imaging (WSI) requires robust data management systems. Efficient storage, retrieval, and processing of these large datasets are critical for seamless integration into clinical workflows. Managing these data sets poses significant challenges in terms of infrastructure, cost, and data security [25].

### Algorithm Performance

DIA algorithms, particularly those based on deep learning, have shown impressive performance, their reliability can be affected by the variability in training data. Algorithms trained on specific datasets may not generalize well to different populations, tissue types, or staining protocols, leading to potential biases and inaccuracies [33].

### Interpretation and Validation

Interpreting and validating the results generated by AI algorithms can be challenging. Pathologists must understand the limitations and potential biases of these tools to ensure accurate

clinical interpretations. Ongoing validation studies are necessary to build confidence in AI-driven diagnostics [42]. Rigorous validation of DIA algorithms is necessary to ensure their accuracy and reliability. This involves extensive testing across diverse datasets and clinical scenarios to assess the robustness and generalizability of the algorithms. However, the lack of standardized validation protocols poses a challenge [32].

### Interpretation of Results

While DIA provides quantitative data, the interpretation of these results requires expertise. Pathologists must understand the underlying principles of the algorithms and be able to integrate quantitative findings with clinical context. This necessitates additional training and expertise [31].

### Regulatory Approval

Gaining regulatory approval for DIA tools can be a lengthy and complex process. Regulatory bodies require comprehensive evidence of safety, efficacy, and clinical utility, which can be challenging to compile, especially for novel algorithms [33].

### Cost and Accessibility

The cost of implementing digital pathology systems can be a barrier for many institutions, especially in low-resource settings. Additionally, ensuring equitable access to advanced diagnostic technologies remains a critical concern [39]. The implementation of DIA requires significant financial investment in digital pathology infrastructure, including high-resolution scanners, powerful computing resources, and specialized software. This can be a barrier, especially for smaller pathology labs and institutions with limited budgets [25].

### Accessibility

Access to DIA technology can be limited in low-resource settings, exacerbating disparities in healthcare. Ensuring equitable access to these advanced diagnostic tools is crucial for broader adoption and impact [15].

### Workflow Integration into Clinical Practice

Integrating DIA into existing clinical workflows can be challenging. It requires coordination between pathologists, IT departments, and administrative staff to ensure smooth implementation and operation. Disruptions to established workflows can hinder the adoption of DIA [25].

### Acceptance and Trust by Clinicians

Building trust in DIA among pathologists and clinicians is essential. There may be resistance to adopting new technologies due to concerns about reliability, accuracy, and potential job displacement. Ongoing education and demonstration of the benefits of DIA are vital for gaining acceptance [31].

### Future Directions

Digital Image Analysis (DIA) in histochemical evaluation of tumor tissue is a rapidly evolving field. Future developments are

expected to further enhance the accuracy, efficiency, and utility of DIA in clinical and research settings. Advances in imaging technology, such as multi-spectral imaging and integration of multi-omics data, are expected to enhance the capabilities of digital image analysis. These innovations will provide deeper insights into tumor biology and improve diagnostic accuracy [36]. Innovations in imaging technology, such as multiphoton microscopy and hyperspectral imaging, are likely to provide richer and more detailed datasets for DIA. These advanced techniques can capture additional layers of information, such as molecular and metabolic data, that can be integrated into DIA for more comprehensive analysis [43]. Combining histopathological data with genomic, transcriptomic, proteomic, and metabolomic data (multi-omics) will enable a more holistic understanding of tumor biology.

DIA platforms that can seamlessly integrate and analyze these diverse data types will be at the forefront of precision oncology [44]. Successful integration of digital pathology into routine clinical practice requires training pathologists, ensuring system interoperability, and developing clinical guidelines. Collaborative efforts among stakeholders will be essential to achieve this goal [24]. As DIA technologies become more refined and validated, their integration into routine clinical diagnostics is expected to increase. Automated image analysis systems will assist pathologists by providing preliminary diagnoses, quantifying biomarker expression, and identifying regions of interest for further review [45]. The adoption of telepathology, facilitated by DIA, will enable remote consultation and collaboration among pathologists in Africa and worldwide. This will be particularly beneficial for resource-limited settings where access to specialized pathology expertise is limited [46].

Future research opportunities include the development of novel biomarkers, predictive models, and studies on rare cancers. Continued innovation in AI and machine learning will drive advancements in digital pathology [31]. Artificial Intelligence (AI) and Machine Learning (ML) will continue to drive discoveries in cancer research. Unsupervised learning algorithms can identify novel patterns and associations in histopathological data, leading to new insights into tumor heterogeneity, progression, and treatment response [33]. DIA will play a crucial role in clinical trials by enabling the precise and reproducible quantification of tissue biomarkers. This will improve the assessment of therapeutic efficacy and the identification of biomarkers for patient stratification [32].

DIA combined with ML can develop predictive models to forecast disease outcomes and treatment responses. These models will be instrumental in personalizing treatment plans based on the specific characteristics of an individual's tumor [47]. Real-Time Analysis: The future of DIA includes real-time image analysis during surgical procedures, such as intraoperative assessment of tumor margins. This will aid surgeons in making immediate decisions, potentially improving surgical outcomes [48]. Training programs incorporating DIA and AI tools will be essential for educating the next generation of pathologists. These programs will focus on the interpretation of digital images and the integration of quantitative



data into clinical practice [33]. Continuous Learning Algorithms: DIA systems that incorporate continuous learning mechanisms will improve over time as they are exposed to more data and feedback from pathologists. This iterative improvement will enhance the accuracy and reliability of these systems [45].

## Conclusion

Digital image analysis has brought significant improvements in the accuracy, reproducibility, and efficiency of histochemical evaluations compared to traditional methods. Its applications span clinical diagnostics and research, offering substantial benefits in cancer care. The integration of Digital Image Analysis (DIA) in the histochemical evaluation of tumor tissue will mark a significant advancement in the field of pathology in Africa. DIA leverages the power of computational algorithms and high-resolution imaging to provide a more accurate, reproducible, and efficient analysis of tumor characteristics, offering substantial benefits over traditional methods. Enhanced Accuracy and Reproducibility: DIA reduces the subjectivity and variability inherent in manual histopathological evaluations. By providing standardized, objective measurements, DIA enhances diagnostic accuracy and inter-observer consistency. Quantitative Analysis: DIA enables precise quantification of histological features, crucial for understanding tumor biology. This includes the measurement of cell density, nuclear size, and biomarker expression, which are essential for prognostication and personalized treatment planning. Efficiency and Workflow Integration: The use of DIA streamlines pathology workflows, reducing the time required for slide review and allowing pathologists to focus on more complex cases. This will improve overall laboratory efficiency and throughput in the continent of Africa.

By providing quantitative and reproducible data, digital pathology enhances cancer diagnosis and treatment planning. It empowers pathologists with advanced tools, ultimately improving patient outcomes. DIA's impact on histochemical evaluation is profound. It not only enhances the precision and speed of diagnostic processes but also supports the discovery of new insights into tumor biology through advanced image analysis techniques. By integrating quantitative data with histopathological evaluation, DIA contributes to more informed clinical decision-making and personalized patient care.

Addressing current limitations and fostering interdisciplinary collaborations will be crucial in realizing the full potential of digital image analysis in the African landscape. The future of pathology lies in the seamless integration of digital and computational technologies. The future of DIA in histochemical evaluation is promising, driven by continuous technological advancements and increased integration into clinical practice as seen in other continents. Emerging technologies, such as advanced imaging techniques and multi-omics integration, are expected to provide even richer datasets for analysis. Additionally, the growing adoption of AI and machine learning will further enhance the capabilities of DIA systems, enabling real-time analysis and predictive modeling [43,49].

## References

1. Della Mea V, Demichelis F (2012) Digital pathology in cancer diagnosis and therapy: Advances and challenges. *Histopathology* 61(1): 16-24.
2. Yibala I Oboma, Benjamin E Susana, Stephen O Elesha, Madukwe Jonathan (2017) Breast cancer biomarkers at Niger delta university hospital: Comparisons with national and international trends and clinical significance Jonathan. *Pathophysiology* 24(3): 191-196.
3. Pantanowitz L, Sharma A, Carter AB, Kurc T, Sussman A, et al. (2018) Twenty years of digital pathology: An overview of progress and potential future applications. *Archives of Pathology & Laboratory Medicine* 142(3): 322-335.
4. Gray A, Wright A, Jackson P, Hale M, Treanor D (2014) Quantification of histochemical stains using whole slide imaging: Development of a method and demonstration of its usefulness in laboratory quality control. *J Clin Pathol* 68(3): 192-199.
5. Bejnordi BE, Timofeeva N, Otte-Höller I, Karssemeijer N, van der Laak JAWM (2014) Quantitative analysis of stain variability in histology slides and an algorithm for standardization. *Proceedings of SPIE - The International Society for Optical Engineering, Medical Imaging 2014: Digital Pathology* 9041: 90410D.
6. Howard FM, Dolezal J, Kochanny S, Schulte J, Chen H, et al. (2021) The impact of site-specific digital histology signatures on deep learning model accuracy and bias. *Nat Com* 12(1): 4423.
7. Underwood JCE (2017) More than meets the eye: The changing face of histopathology. *Histopathol* 70(1): 4-9.
8. Patel A (2020) Benign vs malignant tumors. *JAMA Oncol* 6(9): 1488.
9. Weinstein RS, Graham AM, Richter LC, Barker GP, Krupinski EA, et al. (2009) Overview of telepathology, virtual microscopy, and whole slide imaging: Prospects for the future. *Hum Pathol* 40(8): 1057-1069.
10. Kumar S (2009) Telepathology: An audit. In S. Kumar & B. E. Dunn (Eds.). *Telepathology* pp. 225-229. Springer-Verlag.
11. Petersen JM, Jhala N, Jhala DN (2023) The critical value of telepathology in the COVID-19 era. *Federal Practitioner* 40(6): 186-193.
12. Braunhut B, Graham A, Richter L, Webster P, Krupinski E (2013) Fifth generation telepathology systems: Workflow analysis of the robotic dynamic telepathology component. *Diag Pathol* 8(1): S3.
13. Tizhoosh HR, Pantanowitz L, Al-Jarrah O (2021) Artificial intelligence in digital pathology: A roadmap to routine use in clinical practice. *J Pathol* 254(5): 504-515.
14. LeCun Y, Bengio Y, Hinton G (2015) Deep learning. *Nature* 521(7553): 436-444.
15. Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, et al. (2017) Dermatologist-level classification of skin cancer with deep neural networks. *Nature* 542(7639): 115-118.
16. Lee K, Kim B, Choi Y, Kim S, Shin W, et al. (2018) Deep learning of mutation-gene-drug relations from the literature. *BMC Bioinformatics* 19(1): 21.
17. McKinney SM, Sieniek M, Godbole V, Godwin J, Antropova N, et al. (2020) International evaluation of an AI system for breast cancer screening. *Nature* 577(7788): 89-94.
18. Nagpal K, Foote D, Tan F, Liu Y, Chen PHC, et al. (2020) Development and validation of a deep learning algorithm for Gleason grading of prostate cancer from biopsy specimens. *JAMA Oncology* 6(9): 1372-1380.
19. Liu R, Rizzo S, Whipple S, Pal N, Pineda AL, et al. (2021) Evaluating eligibility criteria of oncology trials using real-world data and AI. *Nature* 592(7855): 629-633.
20. Wang KS, Yu G, Xu C, Meng XH, Zhou J, et al. (2021) Accurate diagnosis of colorectal cancer based on histopathology images using artificial intelligence. *BMC Medicine* 19(1): 76.



21. Clark K, Vendt B, Smith K, Freymann J, Kirby J, et al. (2013) The Cancer Imaging Archive (TCIA): Maintaining and operating a public information repository. *J Digit Imaging* 26(6): 1045-1057.
22. Prior FW, Clark K, Commean P, Freymann J, Jaffe C, et al. (2013) TCIA: An information resource to enable open science. Proceedings of the American Medical Informatics Association (AMIA) Annual Symposium 2076-2085.
23. Lee K, Lockhart JH, Xie M, Chaudhary R, Slebos RJC, et al. (2021) Deep learning of histopathology images at the single-cell level. *Front Artif Intell* 4: 754641.
24. Colling R, Pitman H, Oien K, Rajpoot N, Macklin P, et al. (2019) Artificial intelligence in digital pathology: A roadmap to routine use in clinical practice. *J Pathol* 249(2): 143-150.
25. Zarella MD, Bowman D, Aeffner F, Farahani N, Xthona A, et al. (2019) A practical guide to whole slide imaging: A white paper from the digital pathology association. *Arch Pathol Lab Med* 143(2): 222-234.
26. McClintock DS, Abel JT, Cornish TC (2022) Whole slide imaging hardware, software, and infrastructure. In A. V. Parwani (Ed.), *Whole Slide Imaging* pp: 3-18.
27. Hamilton PW, Bankhead P, Wang Y, Hutchinson R, Kieran D, et al. (2014) Digital pathology and image analysis in tissue biomarker research. *Methods* 70(1): 59-73.
28. Melo RCN, Raas MWD, Palazzi C, Neves VH, Malta KK, et al. (2020) Whole slide imaging and its applications to histopathological studies of liver disorders. *Front Med* 6: 310.
29. Evans AJ, Salama ME, Henricks WH, Pantanowitz L (2018) Implementation of whole slide imaging for clinical purposes: Issues to consider from the perspective of early adopters. *Arch Pathol Lab Med* 142(3): 292-298.
30. Bankhead P, Loughrey MB, Fernández JA, Dombrowski Y, McArt DG, et al. (2017) QuPath: Open-source software for digital pathology image analysis. *Sci Rep* 7: 16878.
31. Madabhushi A, Lee G (2016) Image analysis and machine learning in digital pathology: Challenges and opportunities. *Med Image Anal* 33: 170-175.
32. Saltz J, Gupta R, Hou L, Kurc T, Singh P, (2018) Spatial organization and molecular correlation of tumor-infiltrating lymphocytes using deep learning on pathology images. *Cell Rep* 23(1): 181-193.
33. Komura D, Ishikawa S (2018) Machine learning methods for histopathological image analysis. *Comput Struct Biotechnol J* 16: 34-42.
34. Chang HY, Jung CK, Woo JI, Lee S, Cho H, et al. (2018) Artificial intelligence in pathology. *J Pathol Transl Med* 52(1): 1-12.
35. Janowczyk A, Madabhushi A (2017) Deep learning for digital pathology image analysis: A comprehensive tutorial with selected use cases. *J Pathol Inform* 7: 29.
36. Zhang Z, Wang J (2021) Deep learning for whole slide image analysis: An overview. *Frontiers of Medicine* 15(3): 341-359.
37. Campanella G, Hanna MG, Geneslaw L, Miraflor A, Werneck Krauss Silva V, et al. (2019) Clinical-grade computational pathology using weakly supervised deep learning on whole slide images. *Nat Med* 25(8): 1301-1309.
38. Williams BJ, Hanby A, Millican-Slater R, Nijhawan A, Verghese E, et al. (2017) Digital pathology for the primary diagnosis of breast histopathological specimens: An innovative validation and concordance study on digital pathology platforms. *Journal of Clinical Pathology* 70(1): 108-111.
39. Ho J, Ahlers SM, Stratman C, Aridor O, Pantanowitz L, et al. (2014) Can digital pathology result in cost savings? A financial projection for digital pathology implementation in the US healthcare system. *J Pathol Inform* 5(1): 33.
40. Zhou LQ, Wu XL, Huang SY, Wu GG, Ye HR, et al. (2020) Lymph node metastasis prediction from primary breast cancer by hybrid deep convolutional neural networks. *Journal of Cancer Research and Clinical Oncology* 146(5): 1167-1178.
41. Louis DN, Gerbe GK, Baron JM, Bry L, Dighe AS, et al. (2014) Computational pathology: An emerging definition. *Arch Pathol Lab Med* 138(8): 1133-1138.
42. Daniel C, Oesterling E (2020) Digital pathology and artificial intelligence in hematopathology. *Hematopathology* 35(2): 91-104.
43. Gurcan MN, Boucheron LE, Can A, Madabhushi A, Rajpoot NM, et al. (2009) Histopathological image analysis: A review. *IEEE Rev Biomed Eng* 2: 147-171.
44. Huisman A, van Gils CA, van Diest PJ (2019) Digital pathology: The future of pathology. *Journal of Clinical Pathology* 72(6), 411-417.
45. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, et al. (2016) The 2016 World Health Organization classification of tumors of the central nervous system: A summary. *Acta Neuropathologica* 131: 803-820.
46. Mukhopadhyay S, Feldman MD, Abels E, Ashfaq R, Beltaifa S, et al. (2018) Whole slide imaging and digital pathology: Utilization and challenges in the United States. *Archives of Pathology & Laboratory Medicine* 142(5): 656-674.
47. Litjens G, Kooi T, Bejnord BE, Setio AAA, Ciompi F, et al. (2017) A survey on deep learning in medical image analysis. *Med Image Anal* 42: 60-88.
48. Beck AH, Sangoi AR, Leung S, Marinelli RJ, Nielsen TO, et al. (2011) Systematic analysis of breast cancer morphology uncovers stromal features associated with survival. *Sci Transl Med* 3(108): 108ra113.
49. Huisman A, Looijen A, van den Brink SM, van Diest PJ (2010) Creation of a fully digital pathology slide archive by high-volume tissue slide scanning. *Hum Pathol* 41(5): 751-757.