

Introduction to Digital Pathology for Histological Imaging Analysis in Oncology: Practical Experiences

Introducción a la Patología Digital para el Análisis de Imágenes Histológicas en Oncología: Experiencias Prácticas

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ESCALONA, E.; VEJAR, C.; SEQUEIRA, G. R.; BAZZONI, P. L. & QUIROZ, A. Introduction to digital pathology for histological imaging analysis in oncology: practical experiences. *Int. J. Morphol.*, 44(2):420-430, 2026.

SUMMARY: Telepathology, a branch of telemedicine, enables the remote transmission of pathological images for diagnosis and research. It relies on digital pathology, which converts tissue samples into whole-slide images (WSIs) that can be stored, shared, and analyzed globally. This enhances collaboration among pathologists and reduces workflow and observer variability while maintaining image quality without compromising resolution. This narrative review examines the application of digital pathology in analyzing histopathological images in oncology. We outline key and introductory guidelines for integrating digital pathology into histological workflows, summarizing essential steps and software for image acquisition and processing, and addressing ethical considerations and the role of artificial intelligence. We also highlight practical experiences with digital pathology in routine cancer diagnosis and biomarker assessment, supporting a view of its transformative impact on clinical management. In summary, we discuss benefits and considerations to facilitate the transition from traditional to digital pathology.

KEY WORDS: Digital pathology; Artificial intelligence; Oncology diagnosis; Digital imaging of histopathology; Telepathology.

INTRODUCTION

Telepathology, derived from the advances in technology of telemedicine, allows the remote transmission of histopathological images for diagnostics and research, relying on digital networks to maintain image quality. Digital pathology, the technology behind telepathology, involves converting tissue slide samples into high-resolution digital images known as whole slide images (WSI). These digital images replicate the experience of traditional microscopy, and since its use in clinical trials was comparable to traditional light microscopy according to FDA (Farahani *et al.*, 2015).

Digital pathology workflow applied to histological processes

Digital pathology is extensively used for hematoxylin-eosin slides and cytopathology, with increasing

attention on immunohistochemistry (IHC) (Chen *et al.*, 2017; Kim *et al.*, 2024). IHC image interpretation often requires manual scoring by expert pathologists, which can lead to variability due to individual interpretations. For example, a study examining pathologists' personality traits in relation to PD-L1 assessment found that those with higher conscientiousness exhibited lower variability and higher sensitivity and specificity (Pagni *et al.*, 2020). In contrast, pathologists with higher scores for neuroticism showed reduced specificity and correlation with more PD-L1 positive tumors findings, showing less concordance (Butter *et al.*, 2022). The critical need for technological solutions aimed at minimizing inter-observer variability and enhancing the consistency of pathological evaluations relies on the advancements on digital pathology, which not only allows for the capture and visualization of stained tissue samples in

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Emilia Escalona and Claudia Vejar have contributed equally to this work.

FUNDING. Fondecyt Grant N°11251816 and PAI85250150.

a virtual environment but also enables further computational analyses that bolster diagnostic consistency and expand scalability. As depicted in Figure 1, from the sample to the histopathological slides standards methods are required, then, to transition to digital pathology, the first step is converting these histopathological slides into a reliable digital form that supports remote assessments and collaborative diagnostics, vital for advancing telepathology. Next, the subsequent phases are digital image processing to improve outcomes, segmentation (isolation of relevant pixels), feature extraction, and quantitative analysis of digital data. These stages, outlined in Figure 2, emphasize the necessity of precise reporting and standardized procedures to maintain uniformity across both clinical and research settings, to achieve strong and reproducible outcomes. In digital IHC analyses, specific software and algorithms are required to identify pixels in the processed digital images, allowing the automatic identification of positive/negative markers of interest using standardizable thresholds, put focus on nuclear or cytoplasmic cell areas, or to analyze and compare cell distributions or membranous patterns (Fedchenko & Reifenrath, 2014). Key analyses in IHC include staining intensity (scored 0 to +3 for negative to strong staining) and

proportional score (percentage of positive cells), but different markers require specific focus, like HER2 in breast cancer which emphasizes intensity or Ki-67 which focuses on positivity proportion (Johnson *et al.*, 2021; Ivanova *et al.*, 2024). Common software for image processing includes ImageJ and QuPath, both open-source programs for digital pathology (Bankhead *et al.*, 2017; Schroeder *et al.*, 2021). Fiji, compatible with ImageJ, adds new features and plugins for enhanced usability (Thomas *et al.*, 2021). CellProlifer is another advanced, open-source software notable for automated image scoring and cell analysis (Stirling *et al.*, 2021). Another software programs to digital processing and analysis are summary in Table I. However, while these software solutions enable robust quantitative analysis of IHC markers, the reliability of digital pathology ultimately depends on rigorous validation processes, since discrepancies can occur due to image quality, metadata limitations, or user inexperience. Consequently, still WSI must be systematically compared with conventional glass slides to ensure diagnostic accuracy, reproducibility, and clinical confidence, highlighting the need for WSI quality control to detect artifacts. Recent solutions like automated quality assurance software and large-scale hospital adoption, show that

Digital Pathology workflow

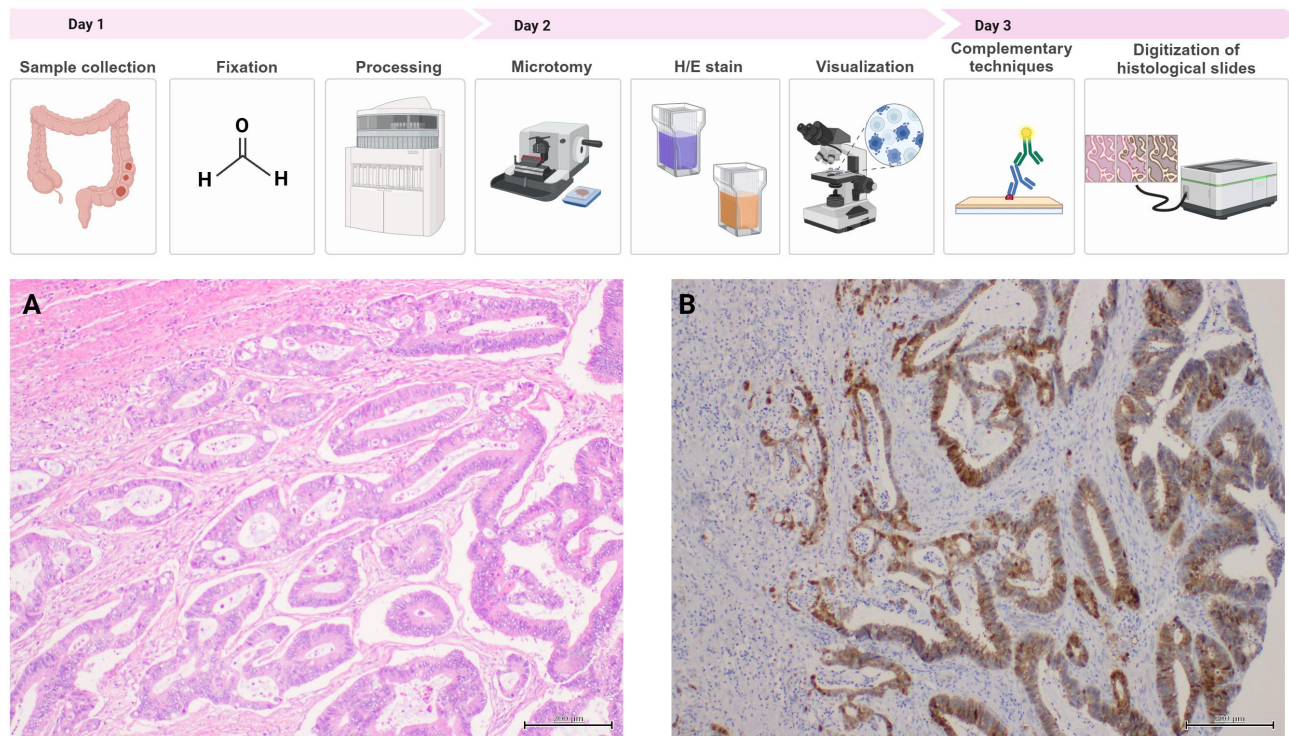


Fig. 1. Digital Pathology Workflow: From Sample Collection to Histological Slide Digitization. In the upper panel, the key stages preceding image digitization are shown, while in the lower panel: (A) Hematoxylin and Eosin staining (H&E), and (B) Immunohistochemistry of β -catenin of colon adenocarcinoma. Created with BioRender.com

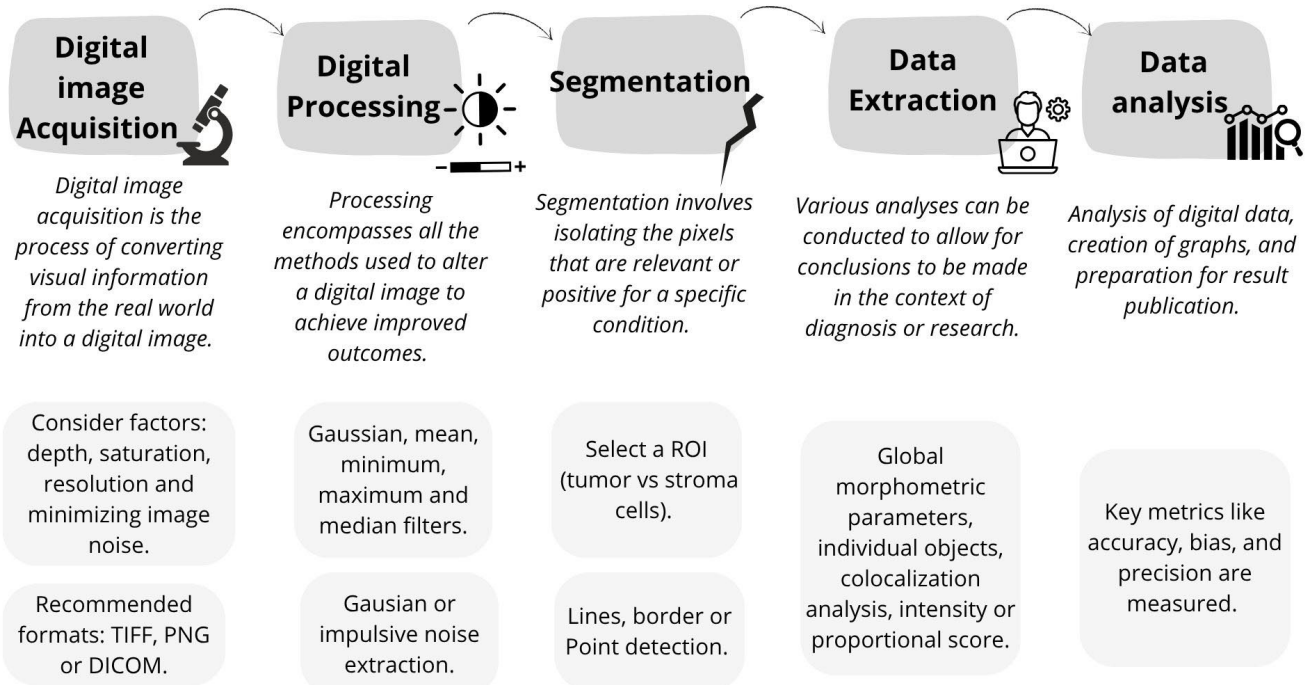


Fig. 2. Phases of Image Processing in histopathology digital analysis. It includes image acquisition, processing, segmentation, data extraction and data analysis.

transitioning to digital pathology reduces variability and enhances efficiency, throughput, and reproducibility, solidifying its importance in modern diagnostics and research (Pantanowitz *et al.*, 2013; Retamero *et al.*, 2020). However, for the safe implementation of WSI systems in routine practice, some regulatory frameworks have been established for the approval and safe implementation of WSI systems in routine practice. College of American Pathologists (CAP) and the Digital Pathology Association (DPA) have issued guidelines for validating WSI systems, emphasizing comprehensive validation of the entire system and recommending institutions conduct their own studies. CAP requires a minimum of 60 cases and a 2-week washout period, while DPA requires 100 cases and a 3-week interval, with additional randomization requirements. The CAP focuses on overall system efficacy, while the DPA emphasizes validation tailored to specific diagnostic applications, prohibiting clinical use outside the validation scope (Pantanowitz *et al.*, 2013). Also, WSI scanners were classified as *in vitro* diagnostic (IVD) medical devices and require a CE mark in the EU under Directive 98/79/EC, ensuring a thorough evaluation of scientific documentation and clinical effectiveness (Evans *et al.*, 2018), and in 2016, FDA give several guidelines for evaluating WSI devices, aimed at ensuring safety and quality control. Companies like Philips, Roche/Ventana, and Leica have products approved as EC-IVD and by the FDA. In April 2017, the FDA approved Philips IntelliSite Pathology Solution (PIPS) for primary

diagnostic use in the US, allowing pathologists to analyze digital images of pathology slides with reduced discrepancies (Evans *et al.*, 2018). These are some of the key recommendations, but it is expected to be constantly updating the avenue of new technologies.

Artificial Intelligence (AI) in digital pathology

Advances in deep learning and the explosion of AI have significantly impacted the field of pathology. AI tools and algorithms have been well received for WSI analysis, as they can process large datasets and detect subtle patterns that might otherwise be missed by the human eye, significantly improving diagnostic accuracy and efficiency. Specifically, in cancer diagnosis, the use of AI offers numerous advantages: 1) AI, particularly deep learning algorithms, increases the accuracy and efficiency of cancer diagnosis by enabling the automatic quantitative assessment of highly complex medical images. 2) AI reduces the workload of pathologists, especially in telepathology, by increasing the efficiency of their daily routines. 3) AI ensures high data reproducibility, which is critical for clinical applications and research. 4) AI improves diagnostic accuracy by extracting and quantifying key information from digital clinical images, contributing to more accurate risk stratification and offering the potential to personalize treatment options. 5) AI reduces intra- and inter-observer variability, mitigating inconsistencies in interpretations and

Table I. Digital software used for clinical-histopathological diagnosis and research.

Software	Description	Uses
3DHistech	SlideViewer is a 3DHISTECH application that allows you to open, view, and analyze digital slides. It is specifically designed for use in research institutions and universities, supporting and enhancing both research and teaching activities. QuantCenter is used for image analysis applications, specifically designed for the quantification process of whole-slide digital images. (https://www.3dhistech.com)	Histological analysis of prostate tissue in patients undergoing aquablation for benign prostatic hyperplasia (Temprana-Salvador <i>et al.</i> , 2022).
QuPath	This open-source software is used for bioimage analysis and digital pathology applications. It offers a complete set of tools for handling whole-slide images, although it is versatile enough to be used with other image formats. (https://qupath.github.io)	IHC analysis of tissues (Bankhead <i>et al.</i> , 2017).
CellSens (Olympus)	It's a platform that allows users to customize and adapt their systems to meet the changing demands of research. With cellSens Dimension, image deconvolution and sharing are made easy. (https://evidentscientific.com/software/cellsens)	Quantification of glomeruli in nephropathy and applications of IF and micronucleus detection (Segebarth <i>et al.</i> , 2020; Yoda <i>et al.</i> , 2024).
Cell profiler	It allows you to work with microarray images, view graphs, normalize data, and classify by phenotype using machine learning. (https://cellprofiler.org)	Digital image processing and training of machine learning classifiers (Carpenter <i>et al.</i> , 2006; Stirling <i>et al.</i> , 2021).
Fiji – ImageJ	Fiji is an image processing package based on ImageJ, equipped with numerous plugins for more complete analysis than Image J. (https://imagej.net/software/fiji/downloads)	Analysis of digital images with IHC, IF or morphometric analysis (Schindelin <i>et al.</i> , 2012).
VisioPharm	This specialized software is designed for digital pathology and facilitates the quantitative evaluation of tissues and cells in biopsies and histological preparations. It supports diagnosis and research by providing accurate measurements and enabling faster and more objective morphological assessments. (https://visiopharm.com)	Digital image analysis with IHC for estrogen receptor and p53, CD25 and CK20 in urothelial carcinoma (Kvikstad <i>et al.</i> , 2024).
Tissue Gnostics	Digital pathology software focuses on tissue image analysis and management. It facilitates the digitization, viewing, and examination of high-resolution images, increasing diagnostic accuracy and optimizing the efficiency of daily workflows. (https://www.tissuegnostics.com)	There are no published uses yet.
Leica Microsystems-Biosystems.	A software and hardware platform used in digital pathology and biomedical research. Its goal is to optimize the process of digitizing, visualizing, analyzing, and managing biological samples, with a focus on histology and pathology. Aivia's AI-powered image analysis software is a deep learning-based segmentation workflow. (https://www.leica-microsystems.com/products/microscope-software/)	There are no published uses for software analysis yet.
Indica Labs-HALO	Image analysis software designed to assist in the examination, quantification, and interpretation of digital tissue sample images, primarily used in histological, immunohistochemical, and other staining methodologies. <i>Indica Labs receives FDA clearance for HALO AP Dx digital pathology platform.</i> (https://indicalab.com/halo/)	Quantification of morphological features and segmentation algorithms in tissue analysis. (Horai <i>et al.</i> , 2019)
Route AI	An artificial intelligence platform designed to facilitate faster and more accurate diagnoses using digitalized images of histological samples. <i>PathAI has received FDA clearance and CE Mark for its AISight digital pathology platform. Dx.</i> (https://www.pathai.com)	Uses of morphometric liver collagen. (Loomba <i>et al.</i> , 2021).
APERIO (Leica Biosystems)	A platform developed by Leica Biosystems for the digitalization, analysis, and management of images of histological samples. <i>Aperio GT 450 DX has received US FDA clearance.</i> (https://www.leicabiosystems.com/digital-pathology/management/aperio-imagescope/)	Histological features in FFPE tissue samples. (Bauer <i>et al.</i> , 2024)
VSlide	Digital pathology software designed to view, analyze, and manage digital slide images of biological samples. (https://www.metasystems-international.com)	It is used to integrate automated analysis of brain tissue technology images (Narayan <i>et al.</i> , 2015).

leading to more consistent diagnoses. 6) AI enables personalized medical strategies thanks to its ability to analyze the unique morphological, textural, and molecular characteristics of each cancer patient, enabling personalized care. 7) Once digital pathology is implemented, the need for specialized technical staff can be diminished (Song *et al.*, 2023; Pulaski *et al.*, 2025). Still, challenges remain, including the need for multicenter datasets, improved interpretability, and seamless integration into clinical workflows (Slabaugh *et al.*, 2023). While AI shows promise in addressing the limitations of current traditional diagnostic methods, more research is needed to standardize and integrate AI-based systems into clinical practice (Girolami *et al.*, 2020). On the other hand, it is important to recognize that implementing an AI algorithm associated with digital pathology requires large amounts of data for validation before it can be adopted in a clinical setting (Yang *et al.*, 2023). Beyond validation efforts, it is also essential to improve workflow efficiency. One promising strategy is through transfer learning, which can also reduce training duration by utilizing existing models that have already been developed and trained and then tailoring them to the specific data being analyzed. This technique involves modifying pre-trained models by altering only specific parameters, such as the affine parameters of the batch normalization layers and the final classification layer. This method improves computational efficiency while maintaining accuracy (Rabilloud *et al.*, 2023). Over the years, the use of AI in medical applications has grown significantly, improving the effectiveness of detection and diagnosis of various types of cancer, including Gleason score analysis and several AI-based software programs have received FDA and CE approval for these purposes (Eloy *et al.*, 2023; Huo *et al.*, 2024; Matthews *et al.*, 2024). In routine diagnosis, a pathologist examines prostate tissue samples under a microscope and assigns two scores to produce a Gleason score, which can range from 2 to 10. This traditional process is time-consuming, labor-intensive, and could show significant variability between different observers (Eloy *et al.*, 2023; Huo *et al.*, 2024). For example, a software called Paige Prostate is an AI tool specifically designed to detect prostate cancer, aiding in this cancer diagnosis. It can evaluate the Gleason score and identify patterns in biopsy samples. This software is continuously updated and has demonstrated a remarkable increase in sensitivity, allowing it to detect cases that were initially missed (Eloy *et al.*, 2023). Another example where the application of AI software optimizes the image analysis workflow is the segmentation of cancerous epithelium, which improves the efficiency and consistency of diagnosis (Faryna *et al.*, 2024), or in cervical cancer, where numerous studies have shown that incorporating AI can improve the accuracy of early diagnoses and treatment applications (Hou *et al.*, 2022). For

example, a study published in 2024 introduced the AICCS system, developed and validated using data from 16,056 participants. Using one AI model for cell detection and another for whole-slide classification, it achieved high accuracy, sensitivity, and specificity. Another observational trial showed that AICCS-assisted cytopathologists significantly improved their sensitivity by 13.3 % and overall accuracy, highlighting its potential as a tool for more efficient and accurate screening (Wang *et al.*, 2024). An important practical consideration is that AI is unlikely to replace human pathologists soon due to legal, ethical, and other factors. However, it can assist in standardization and quality control (Zhu *et al.*, 2024). Studies indicate that combining AI with human pathologists improves diagnostic accuracy, consistency, and efficiency, while reducing overqualification rates and diagnostic time (Eloy *et al.*, 2023). A Delphi survey collected the opinions of 24 experts, including medical specialists and PhDs with expertise in computational pathology and artificial intelligence. Consensus was reached on 141 of the 180 survey items, representing 78.3 %. This study provides a detailed projection for the field of pathology to 2030, predicting the routine use of AI applications for tasks such as detecting lymph node metastases, analyzing mitoses and lymphocytes, and performing quantitative analysis of IHC and IF stains (Berbís *et al.*, 2023). Also, AI analysis helps detect subtle histological changes before clinical symptoms or neoplasias develop, aiding in risk stratification to prioritize patients for closer monitoring or timely interventions. The link between digital image parameters and molecular markers like p53, Ki-67, or cyclin D1 paves the way for multimodal diagnostics, enhancing the understanding of disease behavior and prognosis (Berbís *et al.*, 2023). Consequently, digital biomarkers improve diagnostic accuracy and the management of clinical and histopathological data, leading to more efficient clinical management (Singh *et al.*, 2025).

The widespread adoption of digital pathology faces ethical challenges, such as the protection of patient data, transparency of AI algorithms, and promoting fair access to technology. The ethical use of digital pathology requires clear regulations, responsible practices, and oversight by qualified organizations or committees to ensure compliance (Zhang & Zhang, 2023). Traditionally, histopathology maintained patient privacy by restricting access to physical glass slides and removing identifiable information such as labels. However, digital pathology data can be easily duplicated and shared, necessitating additional privacy actions (Shaw *et al.*, 2024). These actions may include managing access to data, applying de-identification techniques to remove identifiable patient information, and legally requiring third parties to follow secure information governance practices (Shaw *et al.*, 2024). Protecting

sensitive information when sharing datasets containing WSI is and will be crucial to balance openness for reuse and necessary privacy restrictions (Holub *et al.*, 2023). Data should be protected through encryption or organizational strategies such as restricted access and appropriate contracts governing data transfer and processing to ensure AI models do not leak personal information, implementing methods such as Private Aggregation of Teacher Sets (PATE) to mitigate these risks (Papernot *et al.*, 2018). These contracts should clearly outline the purpose and requirements of data processing (Holub *et al.*, 2023).

Examples of the use of digital image analysis in the field of cancer biomarkers

Digital pathology can be applied in routine diagnostic imaging, research, or translational medicine, facilitating the analysis and discovery of morphological biomarkers, clinical trial management, and the search for improved treatment options (Baxi *et al.*, 2022):

Blood vessel analysis: Analyzing microvasculature and assessing angiogenesis are crucial for evaluating tumor aggressiveness and prognosis in various cancer types; however, traditional manual assessments are often time-consuming and inconsistent (Timakova *et al.*, 2023; Karageorgos *et al.*, 2024). AI provides an efficient solution for analyzing extensive tissue structures in WSIs. AI models can extract valuable metrics such as blood vessel location and morphology, which are essential for detecting lymphatic and blood vessel invasion and calculating microvascular density. Deep learning-based segmentation methods are commonly employed to identify areas of interest in WSIs as they can efficiently calculate morphometric parameters and handle varying object shapes and sizes (Timakova *et al.*, 2023). Furthermore, these analyses can be extended beyond the cancer field to studies on granulation tissue formation during wound healing (Li *et al.*, 2017).

Mitosis scoring: Mitotic cell counting is a key routine analysis for diagnosing malignant cancer. This process involves enumerating mitoses within a specific number of high-power fields. Unfortunately, this method is time-consuming and can exhibit inconsistencies due to variations in microscope field size, even at high magnifications (Cree *et al.*, 2021). To improve consistency and accuracy, some studies suggest using an AI-based approach that focuses on counting mitotic figures within a 3 mm² area of the mitotic hotspot. This method provides more reliable and reproducible results, of great relevance in the clinical monitoring of breast cancer, capable of counting according to the tumor area or the number of mitotic figures per 1000 malignant cells (van Bergeijk *et al.*, 2023; Ibrahim *et al.*, 2024).

Tumor-infiltrating lymphocytes (TILs): Tumor-infiltrating lymphocytes (TILs) are important biomarkers for certain cancer types. For example, in triple-negative breast cancer (TNBC), TILs are associated with a good prognosis. However, their semi-quantitative nature and heterogeneity can lead to variability in assessments (Zhou *et al.*, 2021). Machine learning approaches have been developed to improve consistency; however, AI adoption in pathology remains limited due to a lack of real-world validation studies and comparisons between AI models. One research study evaluated ten AI-driven TIL scoring models and revealed variability in their analytical validity. Nonetheless, eight of these models were found to have significant prognostic value for invasive disease-free survival, regardless of the training dataset size. The study emphasizes the need for independent research to validate AI models in the field of computational pathology (Vidal *et al.*, 2024). Another study used the QuPath classifier to differentiate cell types in H&E-stained sections. Five machine-derived TIL variables were analyzed in a discovery set of 171 TNBC cases and subsequently validated in a cohort of 749 patients in four groups. All variables showed significant prognostic associations, and Cox regression confirmed their independent correlation with overall survival. These AI-based TIL variables showed strong prognostic value and are now available for future clinical testing (Bai *et al.*, 2021).

For certain types of cancer, more advanced digital pathology procedures using IHC biomarkers have been established. Some experiences are:

Breast cancer: This cancer is a prevalent disease worldwide and is one of the leading causes of death among women, with some impact also on men (Harbeck *et al.*, 2019). It can be classified into several molecular subtypes: Luminal A, Luminal B, HER2-positive, and TNBC. These subtypes are distinguished based on immunohistochemical labeling of the estrogen (ER) and progesterone receptor (PR) markers, Ki-67, and HER2 (Johnson *et al.*, 2021). This labeling is crucial since breast cancer subtypes can exhibit unique behaviors and prognoses, and the need for specific treatments. Several diagnostic algorithms have been developed to better classify these markers, particularly Ki-67. The Ki-67 proliferation index is an essential marker for prognosis and prediction in breast cancer therapy. However, its manual assessment often faces challenges due to interobserver variability and the lack of standardized procedures. Digital image analysis has emerged as a promising solution to improve the accuracy, consistency, and efficiency in assessing Ki-67 levels (Johnson *et al.*, 2021). One study compared five types of digital analysis methods for assessing Ki-67 in breast cancer (Aperio ePathology, Definiens Tissue Studio, Qupath, an IHC color

histogram algorithm, and piNET) (Dawe *et al.*, 2024). They found that piNET and Qupath correlate most with traditional slide viewing. Furthermore, Qupath achieves the best reproducibility. Unfortunately, all digital assessment methods demonstrated a Cohen's k value below 0.8, indicating that none of these approaches achieved clinically meaningful agreement. Discrepancies were attributed to tumor heterogeneity and variations in algorithms. The main challenges were inter-algorithm variability and inconsistent characterization of cutoff scores, arising from the heterogeneous biology of tumors and different algorithm implementations (Dawe *et al.*, 2024). Still, automated systems such as piNET could play crucial roles in the development of robust and reproducible digital analysis approaches for clinical diagnosis in the future. In another study, comparing digital with traditional analysis, a pathologist manually counted Ki67-positive cells for the proliferation index following the whole-section scoring protocol. On the digital image obtained with the Visiopharm integrative system and the HALO platform, three 0.500 mm² regions of interest (ROIs) were marked in areas of high, medium, and low proliferation. From the analysis of 154 invasive breast cancer cases, high inter-observer agreement was found between traditional and digital analysis (almost 0.94 for both platforms), and even higher inter-platform agreement (0.96). Finally, a study comparing digital analysis with visual assessment in 248 tumors found that IAD detected more Ki-67-positive cells (30 % compared with 22.3 % with traditional visualization) and identified more high-grade tumors (Skjervold *et al.*, 2022). This highlights the need to calibrate diagnostic thresholds when implementing new technologies. Together, these studies illustrate that digital analysis improves the standardization and accuracy of Ki-67 assessments, while emphasizing the need to address algorithmic differences and fine-tune diagnostic criteria for optimal clinical application.

Lung Cancer: Lung carcinomas are the most common type of cancer. Several assays and scoring methodologies have been developed to assess the immunohistochemical expression of PD-L1, which is considered the most reliable predictive biomarker for therapy (Marletta *et al.*, 2022). One study evaluated the extent to which PD-L1 scores, obtained using the open-source software QuPath, align with scores manually assigned by three different pathologists. A classifier was developed using 30 non-small cell lung carcinoma (NSCLC) images and tested on 207 images from 69 NSCLC resection cases. The results demonstrated a strong correlation, with a coefficient of concordance of 0.925. However, the automated scoring system yielded more scores in the 1–49 % range than the manual method, which was statistically significant. The study concluded

that the automated PD-L1 scoring system for NSCLC is as accurate as assessments performed by individual pathologists (Naso *et al.*, 2021). In 2019, advances in IHC testing for PD-L1 in NSCLC using digital slides were reviewed. The objective was to assess PD-L1 protein expression using the Tumor Proportion Score (TPS), which is classified as negative (<1 %), low (1–49 %), and high (>50 %). Most testing used the 22C3 pharmDx kit on the Dako Autostainer system. Cases with higher TPS values showed better agreement, with only 10.8 % disagreement, compared to 32 % in negative cases. The report suggests that digital platforms could improve case sharing, interpretation, and the quality of diagnostic tools. Given the importance of PD-L1 scoring in immunotherapy, virtual slides may improve diagnostic accuracy (Pagni *et al.*, 2020). In another case, a novel retrospective digital pathology method was validated on samples from 340 and 792 NSCLC patients from two avelumab JAVELIN clinical trials. This analysis showed a high correlation between the digital solution and conventional tumor proportion scoring (TPS) of PD-L1 protein expression by IHC. Digital and traditional methods were consistent in survival analyses, demonstrating that higher PD-L1 expression cutoffs correlate with improved overall survival and progression-free survival in patients treated with avelumab. The findings confirm the reliability of digital pathology in biomarker scoring in clinical trials, supporting TPS-based pathological assessment (Mrowiec *et al.*, 2020). Furthermore, considering that lung cancer has the highest incidence rate, teamwork between various diagnostic fields is crucial. Within this framework, digital pathology facilitates the fusion of diverse areas of specialization, including radiology and histopathology, among others (Song *et al.*, 2023). To address this, a comprehensive literature review conducted on multiple research databases (PubMed, IEEE Xplore, dblp, ACM Digital Library, and Inspec) over 15 years (2006–2021) identified 2087 articles focused on the use of AI in cancer prognosis and diagnosis, particularly identifying genetic mutations and translocations in various cancer types, with a specific emphasis on lung cancer (Beretta *et al.*, 2022; Song *et al.*, 2023). AI has proven effective in detecting specific mutations such as *STK11*, *EGFR*, *KRAS*, and *TP53* from WSI. It is also capable of identifying translocations, such as those associated with *NTRK*, with high accuracy, allowing the prediction of genetic associations based on histological images.

Conclusion and future challenges of digital pathology in cancer research and diagnosis

Digital pathology accelerates cancer diagnosis and research through faster image analysis, remote

consultations, and standardized protocols for biomarker detection. Despite its advantages, it faces challenges related to costly technology, system integration, and the need for robust validation of clinical scores. Ensuring that AI and machine learning algorithms are accurately trained is essential to maintain diagnostic reliability and fully realize the potential of digital pathology in improving prognosis and treatment outcomes (Berbís *et al.*, 2023). The incorporation of AI into clinical workflows for predictive oncology medicine has the potential to streamline processes and increase efficiency, shifting the focus from cancer deaths to proactive cancer risk management (Berbís *et al.*, 2023; Singh *et al.*, 2025). This strategy represents a paradigm shift in approaching cancer as a medical condition and a challenge for health preservation. While molecular or histopathological techniques are not routinely applied to all patients, validating digital pathology in a large patient cohort could allow extrapolation of results from standard methods, such as hematoxylin-eosin staining, to provide prognostic value and predict the outcomes of molecular biomarkers. Furthermore, the implementation of digital pathology requires adapting current workflows and training pathologists. This training should focus on preparing future professionals to be highly competent in digital pathology technologies. Key areas of specialization should include programming, digital image and device handling, remote communications, automated analysis, and AI applications, among others (Vos *et al.*, 2025). This training not only develops technical skills but

also fosters familiarity with international regulations, IVD high-quality requirements, and bioethical implications. Finally, establishing robust validation and quality control protocols is essential to ensure the accuracy and reproducibility of digital diagnoses, which were challenged during the COVID-19 pandemic (Hanna *et al.*, 2020). These protocols included the use of reference controls and conducting regular audits to verify system reliability before digital pathology was widely adopted in clinical settings (Hanna *et al.*, 2020). As digital pathology continues to evolve, its integration with AI offers significant opportunities for improving diagnostic accuracy, optimizing workflows, and advancing the field of precision oncology. Furthermore, establishing a universal repository of images, clinical trials, and clinical information could facilitate a unified system for the histological analysis of clinical specimens. Key future challenges for digital pathology are summarized in Figure 3.

In conclusion, the integration of digital pathology into the daily workflow of hospital pathology laboratories has the potential to significantly optimize diagnostic practices and resource management, promote collaboration with subspecialists across different institutions, create valuable repositories for resident and medical student training and transforms the pathology laboratory into a more efficient, interconnected, and future-proof unit, better suited to the growing demand for precision oncology and personalized medicine.

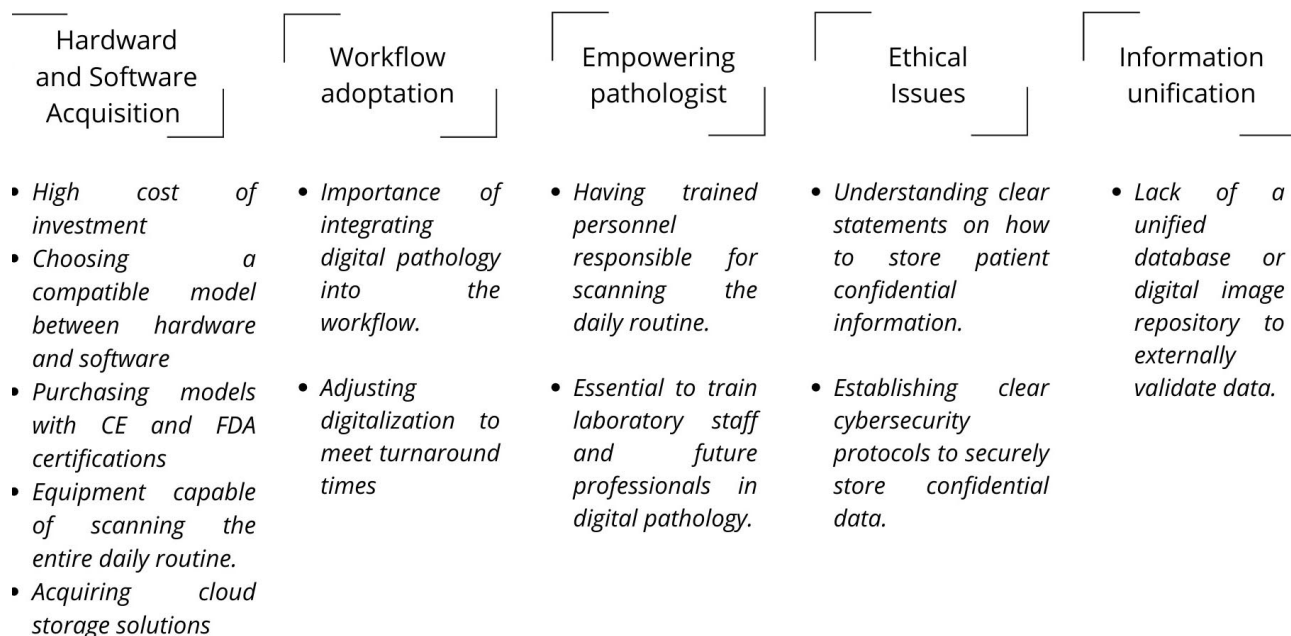


Fig. 3. Future challenges and digital pathology development opportunities.

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RESUMEN: La telepatología, una rama de la telemedicina, permite la transmisión remota de imágenes patológicas para diagnóstico e investigación. Se basa en la patología digital, que convierte muestras de tejido en imágenes de portaobjetos completos (WSI) que pueden almacenarse, compartirse y analizarse globalmente. Esto mejora la colaboración entre patólogos y reduce la variabilidad del flujo de trabajo y del observador, manteniendo la calidad de la imagen sin comprometer la resolución. Esta revisión narrativa examina la aplicación de la patología digital en el análisis de imágenes histopatológicas en oncología. Presentamos directrices clave e introductorias para la integración de la patología digital en los flujos de trabajo histológicos, resumiendo los pasos esenciales y el software para la adquisición y el procesamiento de imágenes, y abordando las consideraciones éticas y el papel de la inteligencia artificial. Asimismo, destacamos experiencias prácticas con la patología digital en el diagnóstico rutinario del cáncer y la evaluación de biomarcadores, lo que respalda la visión de su impacto transformador en el manejo clínico. En resumen, analizamos los beneficios y las consideraciones para facilitar la transición de la patología tradicional a la digital.

PALABRAS CLAVE: Patología digital; Inteligencia artificial; Diagnóstico oncológico; Imagenología digital de histopatología; Telepatología.

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