Perspective

Digital Pathology: Transitioning from Conventional Method to a Data-Driven Future

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Abstract

According to The Royal College of Pathologists, "digital pathology encompasses the acquisition, management, sharing, and interpretation of pathology information—such as slides and data—within a digital framework." While all aspects of clinical pathology, including histological, immunohistochemical, and molecular techniques, can be presented to pathologists after digitization, the college emphasizes that applications of artificial intelligence (AI) in healthcare should be clinically directed with expert input. In the context of this interesting and rapidly evolving field, this article examines the historical development, current workflow, and future potential of digital pathology in a data-driven era and highlights important considerations for integrating digital pathology into established conventional settings in Sri Lanka.

Keywords: Digital Pathology; Artifical Intelligence; Histopathology; Whole Slide Imaging; Sri Lanka

The Historical Roots of Digital Pathology

The Ancient Greeks displayed keen insight by naming the liver "hepar", meaning "to repair oneself", recognizing its remarkable regenerative capacity. This understanding of pathology traces back centuries, with references from Greek mythology, such as Prometheus the Titan, highlighting early perceptions [1]. Over time, scientific advancements have transformed pathology into a refined art form. The invention of the microscope by Antony Van Leeuwenhoek (1632 – 1723) allowed pathologists to observe tissues and cells at the microscopic level, thereby laying the groundwork for diagnostic pathology. However, the limitations of traditional microscopes in observing subcellular particles led to the invention of an electron microscope by Ernst Ruska and Max Knoll in 1931. Despite improvements in lens manufacturing in the early 19th century, there have been no significant advancements in microscopy. By the mid-20th century, mounting tissue samples on glass slides had become a standard practice in pathology laboratories. Pathologists manually examined the slides under a microscope for diagnosis. This traditional approach has remained largely unchanged for many decades [2].

However, in the last decade of the 20th century, the concept of "virtual slides" emerged, revolutionizing the examination of histological sections. This innovation perfectly emulates the traditional microscope and glass slides, allowing the examination of tissue samples at various magnifications without any loss of quality. Initially, digital cameras were attached to the microscopes to capture images of the tissue samples, enabling pathologists to view them on computer screens. However, these early systems had limitations in terms of image quality and resolution. In the 1990s and the early 2000s, significant advancements in scanning technology, particularly digital imaging in pathology, led to the inception and evolution of whole-slide imaging (WSI). WSI enables entire slides to be imaged and stored permanently at high resolution. During the 2000s, dedicated digital pathology platforms began to emerge, offering comprehensive solutions for digitizing, managing, and analyzing pathology images. These platforms integrate slide-scanning hardware with software applications for image storage, retrieval, and analysis. These advancements mark the beginning of a new era in diagnostic pathology called "Digital Pathology," As imaging technology has advanced, researchers have begun to develop automated analysis systems as soon as they can digitize and upload medical images onto computers. From the 1970s to the 1990s, early medical image analysis relied on sequential applications of basic pixel operations (such as edge and line detection and region-growing techniques) and mathematical models (such as line and shape fitting) to create complex rule-based systems designed for specific tasks. This method resembles the expert systems of the era in artificial intelligence, which relied heavily on if-then-else logic [3].

By the late 1990s, supervised methods that used training data to create analytical models had gained traction in medical imaging. Techniques, such as active shape models for segmentation, atlas-based methods (where fitted atlases act as training data), and feature extraction paired with statistical classifiers (for computer-aided detection and diagnosis), have become prominent. This pattern recognition or machine learning approach remains the foundation of many successful medical imaging systems available today.

Naturally, the idea of allowing computers to learn the features that best represent data for specific tasks has led to the development of deep-learning algorithms. These models, built from numerous layered networks, process data inputs (such as images) to deliver outputs (such as detecting disease presence) by progressively identifying higher-level features.

Among deep learning models, convolutional neural networks (CNNs) have emerged as the most effective for image analysis. First applied to medical imaging in 1995 and experiencing significant growth from 2012 onward, deep convolutional networks have become a leading approach in computer vision [4].

Recently, molecular testing has become more prevalent, occasionally replacing the traditional tissue morphological assessments. However, breaking down the tissue for these tests can lead to a loss of crucial histopathological information. These include the host stromal response to malignancy and spatial arrangements, such as the tumor microenvironment, immune reaction to tumors, and rejection events in transplants [5].

Incorporating all these technological advancements now opens up a new dimension with the advent of computational pathology, particularly when integrated with new technologies, such as multiplexing and 3D imaging. We can delve into a detailed analysis of individual pathology image pixels. This approach unveils diagnostic, therapeutic, and potentially unexplored prognostic insights while retaining essential original data for future use [6].

The Workflow of Digital Pathology

The workflow of digital pathology closely aligns with traditional histopathological processes, but includes some key distinctions. Digital pathology fundamentally differs with the use of whole-slide imaging (WSI) and AI-driven image analysis techniques. These innovations allow for digital capture and advanced examination of slides, enhancing diagnostic accuracy, enabling remote collaboration, and introducing efficiencies beyond conventional methods.

Whole Slide Imaging (WSI) is central to digital pathology and allows the creation of comprehensive digital replicas of glass slides. By scanning the slides at a high resolution, WSI preserves the cellular structures and details essential for accurate diagnosis. This enabled pathologists to navigate through images at multiple magnifications, effectively simulating the use of a traditional microscope. This ability to digitally zoom and pan across slides overcomes the constraints of physical slides, increases the diagnostic precision, and enables remote collaboration.

Image analysis further complements WSI by utilizing artificial intelligence (AI) and machine learning to evaluate digital images in ways that extend beyond manual examination. Algorithms are trained to detect, measure, and classify cellular features, and quickly process extensive datasets with minimal observer variability. This efficiency reduces diagnostic bias and promotes consistency, enhancing the overall accuracy of pathological assessments, while supporting rapid and precise diagnostics.

Adhering to the above pivotal steps and incorporating years of scientific research, the current digital pathology workflow can be outlined as follows:

Slide Preparation: Tissue samples were collected and processed, similar to traditional pathology. However, instead of physically mounting slides, they are scanned digitally to generate images.

Slide Scanning: Prepared slides were inserted into a digital scanner to capture high-resolution images of the entire tissue section. These images are digitally stitched to produce complete digital representations of the tissue, known as whole-slide imaging (WSI).

Image Storage and Management: Digital images are securely stored in a database or server and organized for convenient access and retrieval. Each image is typically associated with metadata for reference purposes including patient information and slide identifiers.

Image Viewing, Analysis, and Reporting: This step closely resembles conventional pathology practices. Pathologists use specialized software at computer workstations to access digital images. They can view slides at various magnifications, annotate areas of interest, and conduct measurements and analyses. Diagnostic reports are generated based on their analysis of the digital images

Collaboration, quality assurance, and validation, as fundamental steps, should be conducted in accordance with the guidelines recommended by the Royal College of Pathologist [7].

Future of Digital Pathology in a Data Driven Era

Tremendous advancements in artificial intelligence (AI) have shaped the future of digital pathology. The Royal College of Pathologists (RCPath), in its February 2023 position statement titled 'Position Statement from the Royal College of Pathologists on Digital Pathology and Artificial Intelligence (AI)', outlines its vision and approach in this evolving field. Key points from the statement emphasize that digital pathology and AI can streamline workflows, enhance diagnostic accuracy, and provide free time for pathologists by performing repetitive tasks. However, RCPath stresses that AI applications in healthcare must be clinically directed, and will not replace the expertise and interpretative role of pathologists in diagnosis. Rather, AI serves as a supportive tool to improve efficiency and consistency in pathology, while ensuring that the crucial insights of human pathologists remain at the forefront of patient care [8].

Although the above position statement was published in 2023, discussions about shaping the future perspectives of digital pathology and data-driven technologies within the scientific and medical communities began approximately five years ago [9], and exciting future developments in digital pathology are evident in several key areas.

New digital pathology technologies are enhancing the link between specimen collection and pathology report generation, facilitating a smoother and more efficient data flow. Cutting-edge tools, such as automated multispectral slide imaging for multiplexing, allow the detection of multiple proteins within a single specimen, providing deep insights into tissue complexity. As noted by Kiran et al. [10], this state-of-the-art approach promotes diagnostic accuracy and rapid data access, thereby improving the quality of patient management through more comprehensive and timely pathology reports.

Automated molecular fluorescence tagging and imaging are also breaking new ground by enabling the visualization of proteins at the subcellular level, offering a valuable perspective in cancer pathology [11]. This technique allows for a detailed analysis of cellular environments and tumor heterogeneity, both of which are critical for understanding cancer progression. Research has shown that investigating the molecular profiles of cells using these tools can provide valuable information about tumor biology and facilitate tailored cancer treatments [12]. Moreover, this method enhances our ability to explore therapeutic targets by mapping protein co-expression, signalling pathways, and cell interactions linked to tumor growth and spread.

Quantum dots (qdots) paired with multispectral imaging represent another cutting-edge advancement in gene expression mapping in clinical samples. As photostable nanoparticles with distinctive spectral properties, qdots are ideal for advanced multiplexed imaging, which involves distinguishing multiple biomarkers within a single tissue sample [13]. Tyramide signal amplification, a key element in opal multiplex immunohistochemistry, amplifies detection signals while controlling antibody cross-reactivity, which is especially beneficial for complex assay processes. Incorporating these tools into digital pathology workflows significantly optimizes workloads, enhances diagnostic accuracy, and streamlines the integration of digital images into clinical information systems [14]. Together, these innovations mark a pivotal shift in pathology, making practices more efficient, consistent, and precise, and offering pathologists advanced tools for critical clinical decision making.

Integration of Digital pathology in Sri Lankan context

Incorporating digital pathology into the healthcare sector of a low- to middle-income country such as Sri Lanka presents a nuanced landscape filled with both opportunities and challenges. While the advantages of digital pathology are clear, meticulous attention to details and a multifaceted approach are crucial to the decision-making process. It is important to note that a study conducted at a major academic healthcare institution estimated a potential 5-year total cost saving of $12.4 million for an institution with 219,000 annual accessions, based on anticipated improvements in pathology productivity and histology lab consolidation facilitated by the implementation of an enterprise-wide digital pathology system [15]. This underscores the significance of addressing initial challenges to pave the way for a more efficient future.

One major obstacle is the initial cost of setting up digital pathology infrastructure, which includes the purchase of scanners, software, and storage systems. In a low-middle income country, such as Sri Lanka, where healthcare budgets are limited, securing funding for such investments can be challenging. Moreover, ongoing maintenance and technical support for digital pathology systems require additional resources, which may strain the already stretched healthcare budgets.

Technical complexity is another challenge associated with adopting digital pathology in Sri Lanka. Training health care professionals in the use of digital scanners, image analysis software, and IT infrastructure may require significant time and resources. Additionally, ensuring data security and privacy compliance, particularly in the context of patient health information, is crucial but may require expertise that is not readily available in Sri Lanka's healthcare sector.

Furthermore, regulatory considerations such as the validation and certification of digital pathology systems must be addressed to ensure the safety, effectiveness, and compliance of these systems with quality standards. This may require collaboration with regulatory agencies and investment in capacity-building efforts to meet the regulatory requirements.

Conclusion

Digital pathology, which encompasses the acquisition, management, and interpretation of pathological data within a digital framework, marks a transformative shift from traditional methods. By leveraging artificial intelligence (AI), particularly deep learning models such as convolutional neural networks (CNNs), digital pathology facilitates automated analysis, enhances diagnostic accuracy, and enables remote collaboration, although the interpretative role of pathologists remains essential. Future advancements, including multiplexed imaging, molecular fluorescence tagging, and quantum dots, promise unprecedented diagnostic precision and personalized insights, which are especially valuable in cancer pathology. However, in Sri Lanka, digital pathology faces challenges such as notably high initial setup costs, technical training requirements, and data security concerns. Despite these hurdles, its integration can significantly improve diagnostic efficiency and healthcare outcomes in resource-constrained settings, highlighting the need for thoughtful investments and strategic planning.

Author declaration

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References

[1]. Abu Rmilah A, Zhou W, Nelson E, Lin L, Amiot B, Nyberg SL. Understanding the marvels behind liver regeneration. Wiley Interdiscip Rev Dev Biol. 2019;8(3):1–46.

[2]. Coleman R. Can histology and pathology be taught without microscopes? The advantages and disadvantages of virtual histology. Vol. 111, Acta histochemica. Germany; 2009. p. 1–4.

[3]. Vellino A. Artificial intelligence: The very idea: J. Haugeland, (MIT Press, Cambridge, MA, 1985); 287 pp. Artif Intell [Internet]. 1986;29(3):349–53. Available from: https://www.sciencedirect.com/science/article/pii/0004370286900755

[4]. Litjens G, Kooi T, Bejnordi BE, Setio AAA, Ciompi F, Ghafoorian M, et al. A survey on deep learning in medical image analysis. Med Image Anal [Internet]. 2017;42:60–88. Available from: https://www.sciencedirect.com/science/article/pii/S1361841517301135

[5]. Beck AH, Sangoi AR, Leung S, Marinelli RJ, Nielsen TO, van de Vijver MJ, et al. Systematic Analysis of Breast Cancer Morphology Uncovers Stromal Features Associated with Survival. Sci Transl Med [Internet]. 2011 Nov 9;3(108):108ra113-108ra113. Available from: https://doi.org/10.1126/scitranslmed.3002564

[6]. Van Laak J, Rajpoot N, Vossen D. The Promise of Computational pathology: Part 1. The pathologist. 2018a.

[7]. Cross S, Furness P, Igali L, Snead D, Treanor D. Best practice recommendations for implementing digital pathology. R Coll Pathol [Internet]. 2018;3–5. Available from: https://www.rcpath.org/uploads/assets/f465d1b3-797b-4297-b7fedc00b4d77e51/Best-practice-recommendations-for-implementing-digital-pathology.pdf

[8]. The Royal College of Pathologists. Position statement from the Royal College of Pathologists (RCPath) on Digital Pathology and Artificial Intelligence (AI) [Internet]. 2023. Available from: https://www.rcpath.org/profession/digital-pathology.html

[9]. Castell S, Robinson L, Ashford H. Future data-driven technologies and the implications for use of patient data. 2018;(November). Available from: https://acmedsci.ac.uk/file-download/6616969

[10]. Kiran N, Sapna F, Kiran F, Kumar D, Raja F, Shiwlani S, et al. Digital Pathology: Transforming Diagnosis in the Digital Age. Cureus [Internet]. 2023 Sep;15(9):e44620. Available from: http://www.ncbi.nlm.nih.gov/pubmed/37799211

[11]. Kravchenko Y, Sikora K, Wireko AA, Lyndin M. Fluorescence visualization for cancer DETECTION: EXPERIENCE and perspectives. Heliyon [Internet]. 2024;10(2):e24390. Available from: https://www.sciencedirect.com/science/article/pii/S2405844024004213

[12]. Chakraborty S, Sharma G, Karmakar S, Banerjee S. Multi-OMICS approaches in cancer biology: New era in cancer therapy. Biochim Biophys Acta - Mol Basis Dis [Internet]. 2024;1870(5):167120. Available from: https://www.sciencedirect.com/science/article/pii/S0925443924001091

[13]. Jarockyte G, Karabanovas V, Rotomskis R, Mobasheri A. Multiplexed nanobiosensors: Current trends in early diagnostics. Sensors (Switzerland). 2020;20(23):1–23.

[14]. Yaseen Z, Gide TN, Conway JW, Potter AJ, Quek C, Hong AM, et al. Validation of an Accurate Automated Multiplex Immunofluorescence Method for Immuno-Profiling Melanoma. Front Mol Biosci [Internet]. 2022;9:810858. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35664673

[15]. Ho J, Ahlers SM, Stratman C, Aridor O, Pantanowitz L, Fine JL, et al. Can Digital Pathology Result In Cost Savings? A Financial Projection For Digital Pathology Implementation At A Large Integrated Health Care Organization. J Pathol Inform. 2014;5(1):33.