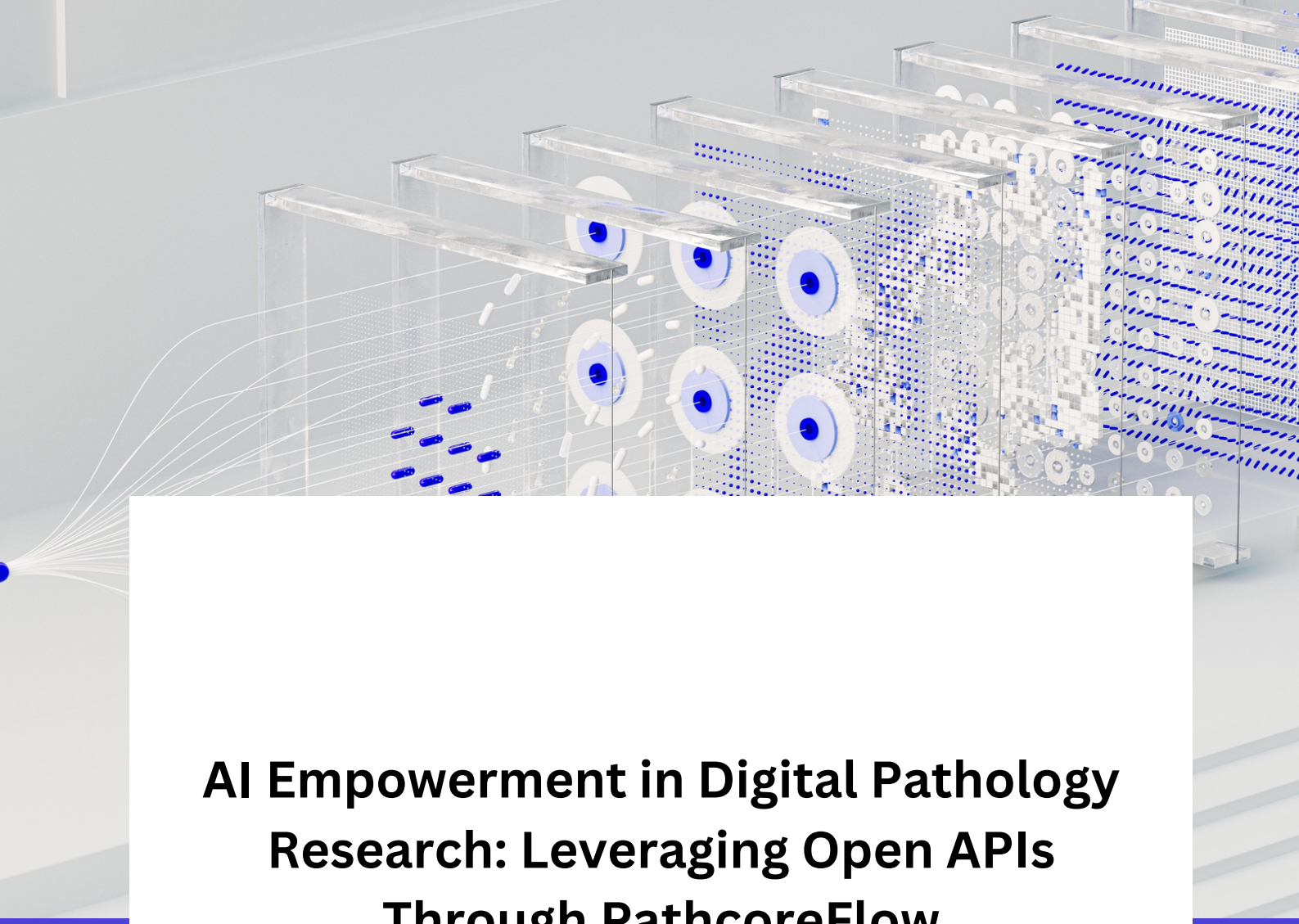

AI Empowerment in Digital Pathology Research: Leveraging Open APIs Through PathcoreFlow

Pathcore & IAMLAB

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Executive Summary

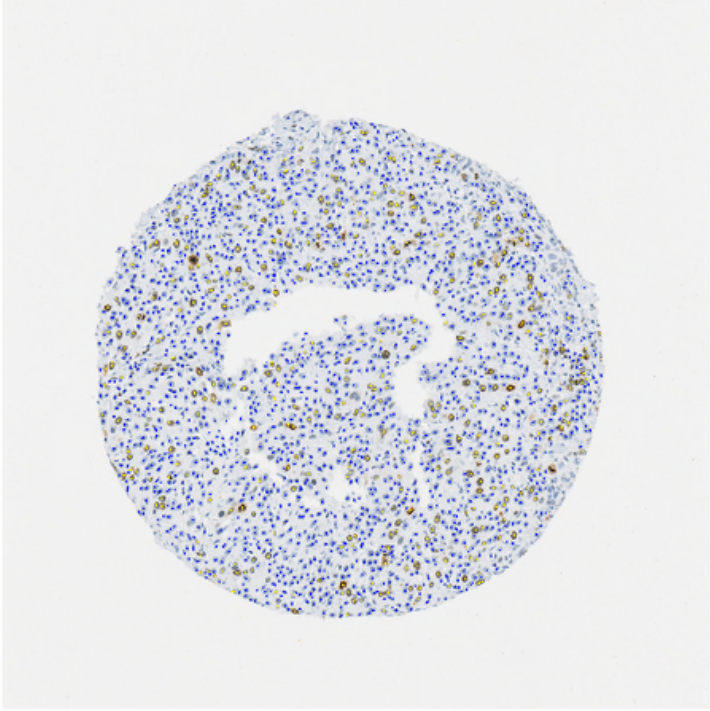
The incorporation of artificial intelligence (AI) into digital pathology research and development is a complex process. Pathologists often encounter challenges such as the subjective and time-intensive analysis of large image datasets. AI emerges as a transformative tool with significant potential to reduce both subjectivity and analysis time. However, applying AI to digital pathology is not without challenges. The nuances of AI integration in digital pathology are explored in this white paper, focusing on how the Image Analysis in Medicine Lab (IAMLAB) is leveraging PathcoreFlow, an open Information Management System with a robust Application Programming Interface (API), to perform research in this field.

PathcoreFlow simplifies data management by allowing seamless access to Whole Slide Images (WSIs), annotations, overlays, and metadata through the cloud, as well as streamlining the collection of annotations from multiple pathologists. It also facilitates the efficient patching of slides for AI studies using tools that leverage the API. An international study involving 90 pathologists conducted by IAMLAB demonstrates that an AI tool integrated into PathcoreFlow significantly improves accuracy, inter-rater agreement, and evaluation time when assessing the Ki-67 biomarker in breast cancer. This white paper illuminates the role of AI in digital pathology research and highlights its potential through PathcoreFlow.

For more information on PathcoreFlow, click here

Introduction and Problem Definition

AI plays a crucial role in digital pathology research and development, including pharmaceutical and human health studies, due to its ability to address various challenges and offer a multitude of benefits. For example, using AI permits the analysis of a large volume of digital images which otherwise would be time-consuming to analyze, with quantitative results that can be distributed and summarized. AI may also be leveraged in clinical workflows to improve turn-around-time (TAT), accuracy and inter-rater agreement of pathologist scoring and grading. Given the pathologist workforce is declining and there is increasing caseloads, pathologist burnout and fatigue are significant problems that AI could help mitigate.



The integration of AI into digital pathology through PathcoreFlow's open Application Programming Interface (API) has the potential to assist research organizations in the analysis of large datasets, improve accuracy through secondary reads and automation of image analysis tasks, as well as reduced diagnostic TAT [1], [2]. As the demand for pathology services continues to rise, AI offers scalability through the analysis of a large number of cases without adding pressure to pathology departments. This can provide motivation for departments to go to a full-scale digital implementation.

Digital pathology images, often referred to as Whole Slide Images (WSIs), present a transformative approach to histological analysis. These images are generated by scanning entire histological glass slides at high resolutions, allowing pathologists to analyze tissue samples on a computer screen. Moreover, the digital format opens up exciting possibilities for utilizing computer-assisted analysis tools for automated quantification [3], [4]. To perform AI development and deployment requires training machine learning models on large datasets of WSI in conjunction with pixel-wise or image-level annotations. In digital pathology applications, these can be especially challenging to obtain and manage.

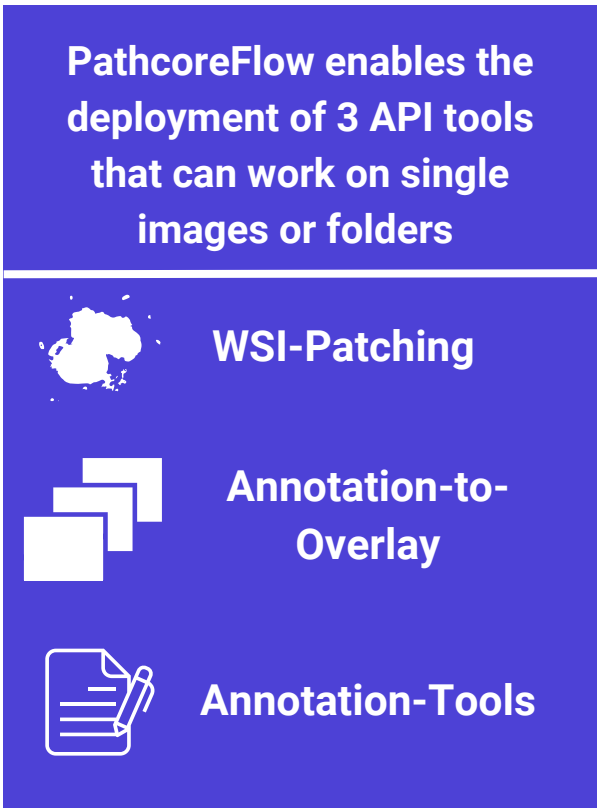
First, WSIs can be extremely large in file size due to a combination of factors, including the scanned resolution, multi-layered images, high color bit-depth, and tiling. Some image sizes can be greater than 5GB with hundreds of thousands of pixels. Consequently, common software systems are insufficient for reading, loading, manipulating and analyzing WSI data. Specialized software is often required to view and process WSI [5]–[10]. Computer systems often face memory restrictions given the large file sizes needed for training digital pathology AI systems. Therefore, patching is usually a first and fundamental preprocessing step whereby WSIs are cut-up into smaller tiles for analysis. Patching optimizes memory use and facilitates AI analyses, paving the way for research and diagnostics.

AI in digital pathology frequently involves supervised learning, wherein an algorithm acquires knowledge from labeled data to discern patterns and make predictions on new, unlabeled data. For instance, deep learning models can be taught to differentiate between normal and tumorous cells from annotations/labels created by a pathologist. However, the creation and management of pathologist annotations for digital pathology AI applications is cumbersome due to the size of the images which makes sharing and accessing them difficult, as well as the lack of annotation standards which creates interoperability challenges.

AI & PathcoreFlow's integration benefits for research organizations	1. **Assist in the analysis of large datasets** 2. **Improve accuracy** 3. **Reduce diagnostic turnaround time (TAT)**

Solution

Dataset size, memory constraints, and annotations are three of the main challenges in the field of AI for digital pathology. These problems are addressed by leveraging the open information management system, PathcoreFlow, along with its powerful API. This combination has enabled the Image Analysis in Medicine Laboratory (IAMLAB) to create a suite of digital pathology tools for research and global collaboration with pathologists. PathcoreFlow is used to upload and share images, overlays, annotations, AI-outputs, and metadata in the cloud, using a seamless, web-based environment. This eliminates the need to store or download WSIs locally via URL(s) that enable data sharing and access. This also simplifies the collection of annotations from pathologists, enhancing the organization and efficiency of data labelling for AI experiments and research.



IAMLAB developed three PathcoreFlow API tools: WSI-Patching, Annotation-to-Overlay, and Annotation-Tools. They work on single images or folders of images. WSI-Patching fetches patches from PathcoreFlow with minimal local resource use and supports various patching options, making it suitable for machine learning tasks such as segmentation and classification. Annotation-to-Overlay converts PathcoreFlow annotations to binary masks and uploads them as overlays. Annotation-Tools is a toolbox for managing PathcoreFlow annotations, allowing bulk actions like uploading, downloading, removal, and modifications to image coordinates, names, descriptions, colors, and visibility status.

A sample training and testing pipeline is shown in Figure 1 for the task of tumour segmentation. First, training slides are uploaded to PathcoreFlow and shared with a pathologist(s) for labelling. The labels are then converted to a binary overlay for each slide. Next, the WSI and corresponding overlays are patched directly from the cloud, and used for training a deep neural network. During testing, the slides are patched, and fed into the trained model for generating predictions all using the PathcoreFlow API. Finally, the predictions are recomposed to the full scale of each respective WSI, and uploaded to PathcoreFlow for easy viewing of the AI results.

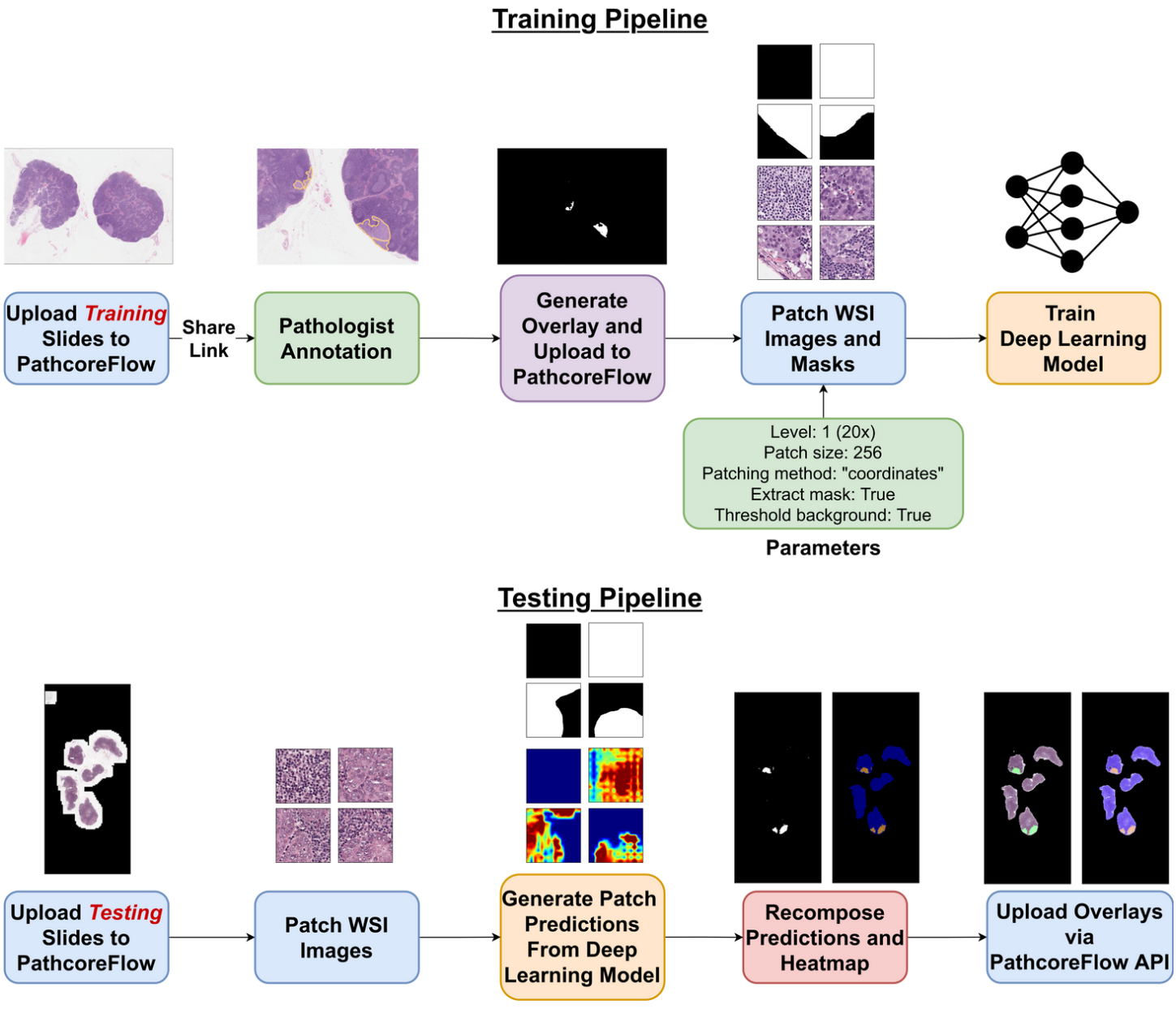


Figure 1: Sample tumour segmentation pipeline from training to testing. PathcoreFlow facilitates the data storage, annotation collection, overlay uploads, and the necessary patching tasks required for computational pathology applications.

Benefits and Outcomes

PathcoreFlow offers a comprehensive solution for the seamless management of digital pathology data, providing numerous benefits to both healthcare professionals and researchers. With its accessibility through browsers and support for leading image formats, it facilitates easy collaboration and analysis. Users can organize their data efficiently by creating folders, storing digital pathology images, and tracking metadata, all while maintaining control over access and permissions. The platform's capacity to share image and folder links, oversee annotations, and automate workflows is enhanced through the integration of a RESTful API with laboratory information systems and image analysis systems, leads to streamlined processes and simplified data management. PathcoreFlow ultimately empowers users to optimize their digital pathology workflows, ensuring efficient and effective collaboration while improving productivity.

"PathcoreFlow ultimately empowers users to optimize their digital pathology workflows, ensuring efficient and effective collaboration while improving productivity."

In an international comparative study involving 90 pathologists, IAMLAB utilized PathcoreFlow to investigate the influence of AI on Ki-67 assessments in breast cancer. Immunohistochemistry (IHC), a technique for visualizing the Ki-67 biomarker, was employed to stain Tissue Microarray (TMA) cores [11]. Pathologists were tasked with evaluating IHC-stained TMA cores for the Ki-67 biomarker by providing the proliferation index (PI), which is the ratio of Ki-67 positive cells to total tumour cells.

Utilizing PathcoreFlow, pathologists scored the digital TMA cores without AI (Figure 2) as well as with the integrated AI tool which displayed semantic nuclei overlays and PI calculations (Figure 3). The scoring performance with and without AI assistance was compared across accuracy, inter-rater agreement and TAT dimensions.

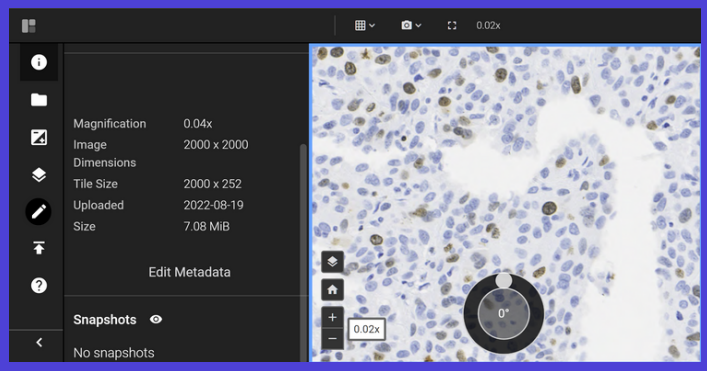


Figure 2: TMA without AI aid.

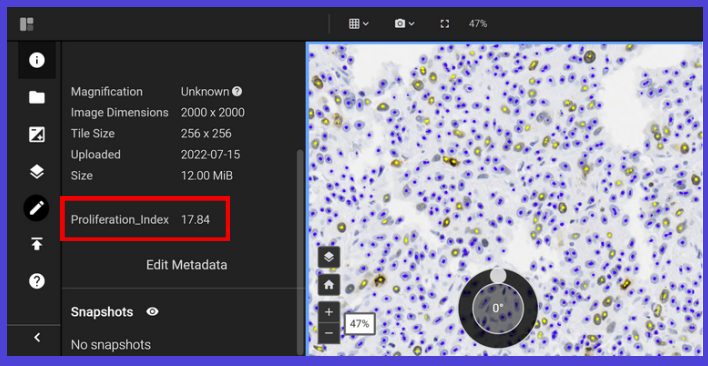


Figure 3: TMA with AI aid.

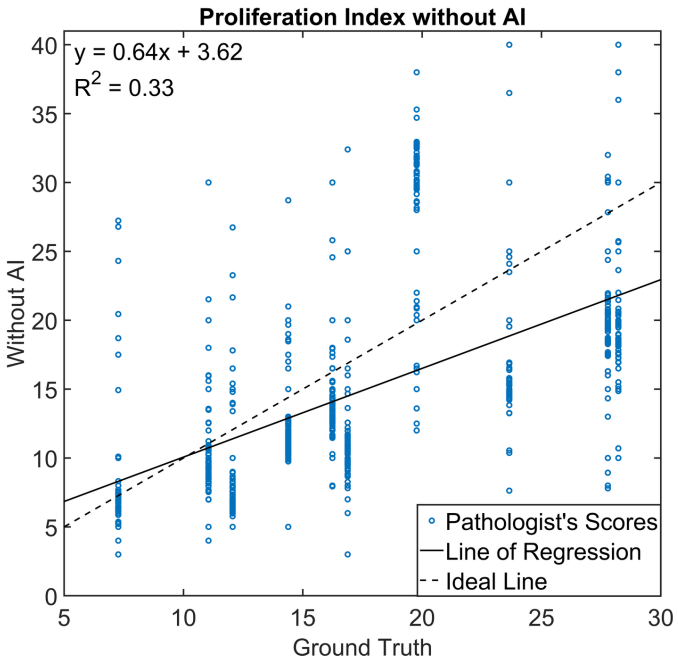


Figure 4: Linear regression demonstrating the relationship between the estimated Ki-67 PI from pathologists without using AI and the ground truth PI.

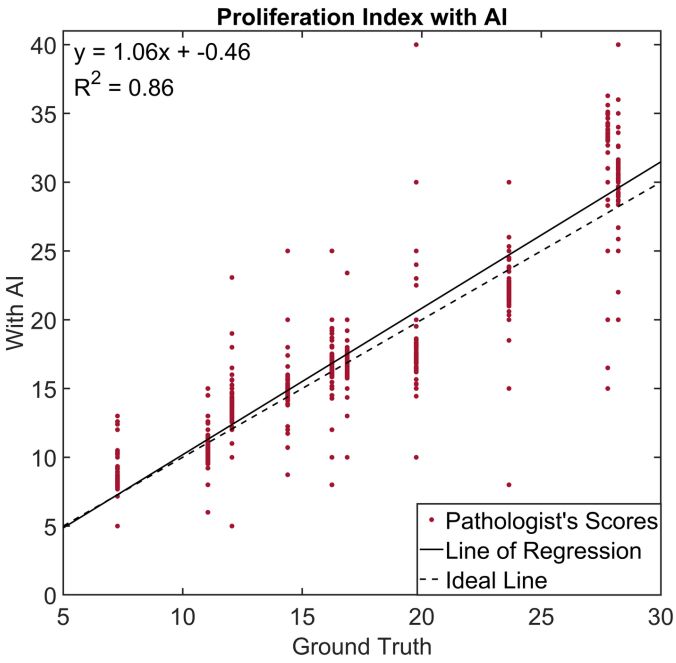


Figure 5: Linear regression demonstrating the relationship between the estimated Ki-67 PI from pathologists using AI and the ground truth PI.

Results of the study demonstrated substantial benefits of using AI, with improved accuracy and inter-rater agreement ($p<0.05$) alongside a reduction in TAT by approximately 5%. Figures 4 and 5 emphasize the advantages of AI in improving pathologist consensus when using AI. There was near ideal agreement (1.06 for the slope and -0.46 for the intercept) when AI was used, which is a substantial improvement compared to the 0.58 slope and a 3.62 intercept without AI assistance. Furthermore, there was an increase in the R-squared values — from 0.33 without AI to 0.86 with AI — indicating a considerable reduction in scoring variability with AI.

This study will be highlighted at the Pathology Visions 2023 conference and has previously been presented at the Pathology Informatics Summit 2023 conference [12], [13]. Its successful execution is attributed to the superior hosting and data-sharing functionalities of PathcoreFlow, enhanced through API integration that streamlined annotation, overlay, and metadata management processes.

Conclusion

The integration of AI into digital pathology research, as exemplified by IAMLAB's international study involving 90 pathologists, marks a significant advancement in the field. The use of PathcoreFlow as a foundational platform, coupled with the open API, has streamlined the workflow and improved the accuracy and efficiency of Ki-67 assessment in breast cancer. The findings underscore the potential for AI to revolutionize the practice of pathology, offering scalable solutions that address challenges related to image analysis, inter-rater agreement, and data management. IAMLAB's development of three PathcoreFlow API tools—WSI-Patching, Annotation-to-Overlay, and Annotation-Tools—further enhances the utility of this platform. As the demand for pathology services continues to grow, the combination of PathcoreFlow and AI is set to provide valuable tools for healthcare professionals and researchers, ultimately driving advancements in the field of pathology and improving patient care.

About the author and IAMLAB

The Image Analysis in Medicine Lab (IAMLAB), led by Dr. April Khademi, is at the forefront of integrating AI into digital pathology workflows, aimed at enhancing research and clinical tasks. Partnering with renowned healthcare institutions, IAMLAB accesses diverse datasets to develop AI-powered diagnostic tools, focusing on innovative biomarkers and aiding in informed cancer treatment decisions.

IAMLAB maintains a collaborative setting, valuing clinician input coupled with engineering design to optimize knowledge-translation opportunities. With a deep commitment to promoting trust in AI applications in medical imaging, the lab advocates for the accelerated adoption of next-generation diagnostic tools, working towards broader acceptance in the healthcare sector and ultimately improving patient care.

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