REVIEW ARTICLE

Digital Image Analysis and Artificial Intelligence in Lung Cancer Pathology

Análise de Imagens Digitais e Inteligência Artificial na Patologia do Cancro do Pulmão

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https://doi.org/

Declaração de Contribuição/Contributorship Statement:

BS and VA: Conception, drafting and review of the work. All authors approved the final version to be published.

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Recebido/Received: December 23rd, 2024

Aceite/Accepted: December 24th, 2024

Publicado online/Published online: December 31st, 2024

Publicado/Published: December 31st, 2024

THE DIGITAL TRANSFORMATION OF PATHOLOGY

Pathology has long been regarded as the "ground truth" in medicine, providing the definitive diagnosis that informs all subsequent clinical decisions. In recent years, the field has experienced a significant digital transformation, opening the door to numerous innovations. Whole slide scanners, introduced in the 1990s, are now present in many pathology departments, enabling high-resolution scanning of entire tissue slides. The benefits of digital pathology systems extend well beyond simple on-screen image viewing. Although these systems are not yet widely adopted for routine clinical diagnosis in Portuguese hospitals, they offer substantial advantages by centralizing data organization and storage, streamlining processes through integrated digital workflows, and enabling convenient sharing of image data.

This digital transformation is only beginning to reveal its full potential, especially as the growth of artificial intelligence (AI) has closely paralleled the digital transformation in pathology, bringing significant advancements to the field. AI, a branch of computer science, aims to develop systems that simulate human intelligence, with machine learning (ML) as a subset focused on recognizing patterns and making data-driven predictions, including deep learning, which uses multi-layered neural networks inspired by the human brain.

Digital image analysis and AI in pathology primarily focus on two areas: (1) Diagnostic Assistance/Computer-aided Diagnosis and (2) Prognostic and Predictive Insights and Biomarker Analysis. In the following sections, we will highlight examples of ongoing developments in these areas, with a focus on lung cancer, that hold promise for near-term implementation in clinical practice.

1. DIAGNOSTIC ASSISTANCE / COMPUTER-AIDED DIAGNOSIS

AI has the potential to significantly enhance one of the most critical tasks in pathology—histopathological diagnosis — which inherently involves a degree of subjectivity in interpreting architectural patterns and cellular features. Even seemingly straightforward tasks, such as distinguishing between normal and neoplastic tissue or differentiating adenocarcinoma (LUAD) from squamous cell carcinoma (SCC), can be challenging. AI models have been developed to assist with these tasks, achieving performance comparable to pathologists' evaluations.[1-5] This advancement not only aids in diagnosis and standardization but also can reduce the need for additional immunohistochemical studies, saving time and resources.

Another noteworthy application of AI in diagnostic classification includes algorithms capable of identifying distinct growth patterns such as acinar, micropapillary, solid, and cribriform, which hold prognostic significance in surgically resected cases.[4] Additionally, AI has shown promise in detecting tumor spread through air spaces (STAS), a unique metastatic pattern that impacts prognosis but is often misdiagnosed and exhibits low interobserver agreement.[6,7]

AI also enhances diagnostic accuracy in cancer staging by improving the detection of lymph node metastases.[8] These tools can increase sensitivity by highlighting areas that require the pathologist's close attention, reducing the risk of missed metastases.

2. PROGNOSTIC AND PREDICTIVE INSIGHTS AND BIOMARKER ANALYSIS

Beyond diagnostic support, AI algorithms can offer prognostic insights by identifying patterns linked to disease progression by identifying patterns associated with disease progression, aiding in risk stratification. For example, models performing quantitative histomorphometry analyze features such as nuclear shape and cellular texture to predict survival or recurrence.[9,10] More disruptively, AI can identify clinically relevant biomarkers and driver mutations (e.g., EGFR, ALK, ROS1, RET) directly from H&E slides, enabling predictive models that link tumoral cell morphology to targeted therapies.[11]

Immunohistochemical evaluation of PD-L1, essential for determining eligibility for PD-1/PD-L1 inhibitors, is another area where AI shows promise. AI models assessing tumor proportion scores (TPS) for PD-L1 expression have demonstrated strong correlations with pathologists' evaluations, offering a more standardized and less error-prone alternative.[12-14]

Tumor-infiltrating lymphocytes (TILs), a prognostic biomarker linked to response to pembrolizumab in advanced NSCLC, can also benefit from AI. Automated TIL quantification reduces inter-observer variability, enhancing reliability.[15,16] Additionally, AI-driven mapping of tumor microenvironment interactions adds prognostic value by uncovering relationships between cells that are otherwise challenging to analyze manually.[13]

CHALLENGES IN AI

Despite its promising potential, integrating AI into pathology poses several challenges. First, the volume of data generated by digital slides is immense; for instance, a single 22 mm x 75 mm slide digitized at 0.25 μm per pixel can generate files up to 90 GB. This data explosion introduces significant technical and storage challenges that require advanced solutions to manage and process effectively.

Additionally, implementing AI in pathology faces logistical challenges, including the need for extensive, and many times annotated datasets for training and the consistency in digital slide quality across institutions. Collaborative efforts to create standardized protocols and robust datasets are critical to overcoming these obstacles.

A key challenge is the "black box" nature of deep learning algorithms, which produce accurate predictions without explaining their reasoning. This lack of transparency can complicate clinical decisions and raise ethical concerns. For example, pathologists may hesitate to trust an AI model that flags a tissue as high-risk without a clear explanation. Addressing this requires research into whether this interpretability gap hinders adoption and, if so, the development of transparent algorithms to build trust and confidence in AI tools.

The adoption of AI tools also requires validation on diverse populations, as errors or biases can directly impact patient outcomes. Integration into clinical workflows across institutions remains difficult due to costs, organizational hurdles, data security requirements, and the need for reliable storage of large datasets. Most current AI tools have been validated on retrospective data, which does not always reflect real-world scenarios. Prospective studies and randomized controlled trials will be critical for broader clinical adoption.

CONCLUSION

Artificial intelligence has the potential to transform pathology, including in lung cancer, by improving diagnostic accuracy, providing better prognostic insights, and supporting therapeutic decisions. When combined with traditional pathology practices, AI can streamline workflows, reduce errors, and ultimately lead to better patient outcomes.

This review presented a few illustrative examples of promising research that are already making a significant impact on the field.

These studies, along with many others not discussed here, are highly valuable as they not only advance our understanding of AI applications in pathology but also have the potential to transform our knowledge of lung cancer itself. They may reshape the future of pathological tissue evaluation and revolutionize diagnostic approaches.

Nonetheless, the applications discussed still require extensive validation and testing to ensure their readiness for widespread clinical adoption. Despite these challenges, the potential of AI in pathology remains undeniable, offering a transformative and promising future for the field.

Previous Presentations: *This article is based on a presentation delivered at the 2nd Portuguese Lung Cancer Congress, held from October 24 to 26, 2024, at the MH Atlântico Hotel in Peniche.*

Ethical Disclosures:

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financial Support: This work has not received any contribution grant or scholarship.

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

Responsabilidades Éticas:

Conflitos de Interesse: *Os autores declaram não possuir conflitos de interesse.*

Suporte Financeiro: *O presente trabalho não foi suportado por nenhum subsidio o bolsa ou bolsa.*

Proveniência e Revisão por Pares: *Não comissionado; revisão externa por pares.*

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