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From whole-slide images to multimodal diagnostics: Foundation models, spatial omics and generative AI in pathology and laboratory medicine

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Abstract

Digital pathology, alongside the revolution of Artificial Intelligence (AI), molecular profiling, spatial omics, liquid biopsy, and multimodal computational systems, is revolutionizing both pathology and laboratory medicine. Conventional pathology is based mainly on the generation of morphological information, and only the interpretation of this morphological information is the expertise of a specialist, while in laboratory medicine it is possible to generate large amounts of biochemical, haematological, microbiological and molecular information. By combining these data streams one can make the shift from single instances of diagnosis towards a more complete, computer aided disease characterisation. The acquisition of WSIs has paved the way for machine-learning solutions for tissue segmentation, tumor detection, grading, biomarker quantification and prediction of prognosis. But, traditional image category-specific models are still constrained by the need for annotations, lack of cross-scan or cross-staining transfer, and also domain variations, which come from different scanner types, staining, tissue-prep, and patient types. Pathology Foundation Models like UNI, CONCH, Virchow, Prov-GigaPath provide transferable representations that can aid various downstream tasks. Generative and multimodal AI also facilitates the integration of histological images with the pathology report, clinical information and molecular findings. Spatial transcriptomics and proteomics enable providing molecular information in the anatomic context, and liquid biopsy can be used to allow for minimal invasive longitudinal monitoring. However, there are challenges to clinical translation, such as bias, interpretability, automatism bias, cyber security, regulation and replicability. In this narrative review, the converging technologies and the opportunities for re-shaping precision diagnostics are discussed. This new paradigm is focused on AI-enabled rather than AI-depleted patho-lab skills

Keywords: *Digital pathology, Computational pathology, Artificial intelligence, Foundation models, Generative AI, Spatial omics, Laboratory medicine, Liquid biopsy, Precision diagnostics, Multimodal AI*

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1. Introduction

Pathology and laboratory medicine provide a substantial proportion of the objective evidence used for diagnosis,

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prognosis and therapeutic decision-making. Histopathology characterizes disease through tissue architecture and cellular morphology, while clinical laboratory disciplines generate quantitative information from blood, urine, body fluids, microorganisms and molecular analytes. Historically, these information streams have been interpreted within relatively separate workflows. The rapid digitization of pathology and increasing availability of computational methods are now creating opportunities to connect morphology, molecular measurements, laboratory results and clinical context within a common analytical framework (Albahra *et al.*, 2023).

Digital pathology has provided the technological substrate for this transformation. Whole-slide imaging converts glass slides into high-resolution digital representations that can be stored, transmitted, searched and analyzed computationally. Beyond enabling remote review and telepathology, digitization makes it possible to quantify morphological features across an entire specimen and to apply machine-learning algorithms at multiple spatial scales (Niazi *et al.*, 2022). The clinical value of digital pathology, however, depends on workflow integration, validation, interoperability, image quality, storage, cybersecurity and local laboratory requirements rather than on scanning alone (Hanna *et al.*, 2022).

Deep-learning methods initially focused on narrowly defined tasks such as tumor detection, metastasis identification, tissue segmentation and biomarker quantification. These systems demonstrated substantial potential, but their dependence on large labeled datasets and their sensitivity to differences in image acquisition limited their portability across institutions. Computational pathology therefore increasingly shifted toward weakly supervised learning, self-supervised learning and representation learning, allowing models to extract useful features from large numbers of unlabeled or weakly labeled slides (Lu *et al.*, 2021).

A more recent development is the emergence of pathology foundation models. These models are trained on very large datasets and are designed to generate representations that can be reused across multiple downstream tasks. Their development is changing the research question from whether an algorithm can solve one pathology problem to whether a general-purpose model can support many diagnostic and prognostic applications (Lu *et al.*, 2023).

The expansion of multimodal AI further changes the diagnostic landscape. Pathology interpretation rarely depends on morphology alone; patient age, clinical history, imaging, immunohistochemistry, molecular findings and previous reports may influence the final diagnosis. Pathology-specific vision-language systems can potentially connect these information sources and support interactive diagnostic reasoning (Lu *et al.*, 2024). Spatial transcriptomics and other spatial-omics approaches add a further dimension by linking molecular states to their anatomical location, while liquid biopsy provides longitudinal molecular information that may complement tissue-based diagnosis (Jain and Eadon, 2024; Tivey *et al.*, 2022).

This narrative review synthesizes recent developments across these interconnected areas, with emphasis on the transition from task-specific digital pathology to multimodal computational pathology and AI-enabled laboratory medicine. The review also considers barriers to implementation and proposes a future framework in which pathology images, molecular data, spatial information, circulating biomarkers and routine laboratory measurements are interpreted as components of a coordinated diagnostic ecosystem.

2. Review approach

This narrative review focused on peer-reviewed literature published predominantly from 2021 through 2026. Literature was identified using PubMed/MEDLINE, Scopus-indexed publications and major biomedical journals, with additional citation chaining for influential recent studies. Search concepts included digital pathology, computational pathology, whole-slide imaging, artificial intelligence, machine learning, foundation models, generative AI, vision-language models, spatial transcriptomics, spatial omics, liquid biopsy, circulating tumor DNA and artificial intelligence in laboratory medicine. Priority was given to recent reviews, methodological studies, large-scale foundation-model papers and clinically relevant investigations. Because this was a narrative rather than systematic review, formal risk-of-bias scoring and meta-analysis were not undertaken.

3. Digital pathology as the infrastructure for computational diagnosis

The transition from glass slides to whole-slide imaging is the foundation on which modern computational

pathology has developed. Digital slides can be reviewed remotely, shared across institutions and subjected to quantitative analysis. Whole-slide images also preserve tissue information across a much larger field than the manually selected microscopic fields commonly used in conventional workflows. This expanded data availability makes automated detection, measurement and spatial analysis possible.

Implementation is nevertheless a laboratory transformation rather than a simple technology purchase. Successful digital workflows require validated scanners, image-management systems, storage capacity, adequate displays, network infrastructure, laboratory information-system integration and quality-assurance procedures. Evidence accumulated during the last several years indicates that digital pathology can achieve high diagnostic concordance when appropriately validated, but validation must account for the local specimen mix, hardware, software and workflow.

Computational pathology builds on this infrastructure by converting image information into quantitative representations. Early applications included nuclear segmentation, tissue classification and tumor detection. Deep learning subsequently expanded these capabilities to biomarker scoring, prognostic prediction, molecular phenotype inference and treatment-response estimation. The growth of weakly supervised methods has been particularly important because complete annotation of a gigapixel whole-slide image is impractical. Multiple-instance learning approaches can instead learn from slide-level labels while identifying diagnostically informative regions.

Despite impressive benchmark performance, the translation of computational pathology into routine practice remains slower than the pace of algorithm development. Major barriers include external validation, domain shift, uncertainty estimation, regulatory requirements, interoperability and the need to demonstrate clinical utility rather than technical accuracy alone (Komura and Ishikawa, 2021). This distinction is important because a model that performs well on a curated dataset may not necessarily improve diagnostic decisions in a real laboratory.

4. From task-specific algorithms to pathology foundation models

Task-specific AI models generally learn a direct relationship between an input image and a predefined output. This approach is useful when the task is clearly defined, but it requires separate development, annotation and validation for different diagnostic questions. Foundation models aim to address this limitation by learning broad representations from very large datasets and subsequently adapting them to downstream tasks with comparatively limited labeled data.

UNI represented an important milestone in this transition. The model was pretrained using more than 100 million histology image patches derived from more than 100,000 whole-slide images and demonstrated transferable performance across diverse computational pathology tasks (Chen *et al.*, 2024). CONCH extended the concept into vision-language learning by aligning pathology images with textual descriptions, enabling applications that require semantic relationships between visual and textual information (Lu *et al.*, 2024).

Virchow further increased the scale of pathology pretraining, using approximately 1.5 million whole-slide images and demonstrating strong performance across a range of pathology tasks, including rare cancer-related applications (Vorontsov *et al.*, 2024). Prov-GigaPath subsequently demonstrated a whole-slide foundation-model strategy using approximately 1.3 billion pathology image tiles from more than 170,000 whole-slide images, illustrating how large-scale pretraining can be combined with architectures designed to preserve whole-slide context (Xu *et al.*, 2024).

Another important development is the use of foundation models for both diagnosis and prognosis. A pathology foundation model reported in Nature demonstrated that a single pretrained representation could support cancer diagnosis and prognosis prediction across multiple cancer types, reinforcing the concept that histological morphology contains information that can be reused for several clinically relevant tasks (Wang *et al.*, 2024).

The increasing availability of pathology foundation models changes the economics of model development. Instead of repeatedly training new models from scratch, investigators can use a pretrained representation and fine-tune or evaluate it on a specific dataset. This may be particularly valuable for rare diseases, where large annotated cohorts are difficult to assemble. However, transferability should not be assumed. Foundation

models remain dependent on their training distributions, and independent benchmarking is necessary to establish whether performance remains robust across scanners, institutions, populations and tissue-processing protocols (Ochi *et al.*, 2025).

Table 1: Representative recent developments in computational pathology and multimodal AI

Technology/model	Core concept	Potential pathology application	Key limitation
Digital whole-slide imaging	High-resolution digitization of complete slides	Remote diagnosis, archiving, quantitative image analysis	Infrastructure, validation and storage requirements
Weakly supervised learning	Learning from slide-level labels	Tumor detection, grading and biomarker prediction	Dependence on label quality and cohort composition
UNI	Large-scale self-supervised pathology representation	Transfer learning across pathology tasks	External validation and domain shift
CONCH	Pathology vision-language representation	Image-text retrieval and multimodal analysis	Need for high-quality paired image-text data
Virchow	Large pathology foundation model	Diagnosis, rare-cancer classification and downstream tasks	Large-scale computational requirements
Prov-GigaPath	Whole-slide foundation modeling	Cancer classification and pathomics	Clinical deployment and infrastructure
PathChat	Generative pathology vision-language model	Interactive diagnostic assistance	Hallucination, uncertainty and human oversight
Spatial omics + AI	Molecular mapping within tissue context	Tumor heterogeneity and microenvironment analysis	Cost, complexity and standardization
Liquid biopsy + AI	Longitudinal molecular monitoring	Minimal residual disease and treatment monitoring	Low analyte abundance and interpretation

5. Multimodal and generative AI in pathology

Pathology diagnosis is inherently multimodal. A pathologist may integrate morphology with immunohistochemistry, molecular findings, imaging, age, clinical presentation and previous pathology. Conventional image classifiers usually operate on only one component of this information. Multimodal AI attempts to bridge this gap by jointly modeling images and language or by integrating multiple data modalities within a shared representation (Xiang *et al.*, 2025).

PathChat is a prominent example of pathology-specific multimodal generative AI. The system combines a pathology vision encoder with a large language model and was fine-tuned using more than 450,000 visual-language instructions. It demonstrated strong performance on diagnostic questions and open-ended pathology queries, illustrating the feasibility of an interactive AI assistant designed specifically for pathology rather than a general-purpose chatbot.

Clinical context may substantially influence multimodal performance. When age, sex, clinical history and radiological information were incorporated into pathology AI evaluation, diagnostic performance improved in comparison with image-only assessment (Marchal, 2024). This observation supports a broader principle: the diagnostic value of a pathology image cannot always be separated from the patient context in which it was generated.

Generative AI also has potential applications in report drafting, case summarization, educational support, differential-diagnosis generation and retrieval of relevant diagnostic information. Nevertheless, these systems introduce a different risk profile from conventional classifiers. A generative model can produce fluent but unsupported statements, omit important findings or express uncertainty poorly. Reviews of large language models in digital pathology therefore emphasize accuracy, privacy, reproducibility, terminology and human oversight as major implementation considerations (Ullah *et al.*, 2024).

Pathology-specific models are likely to be more useful than general-purpose models for specialized clinical tasks because pathology requires domain-specific terminology, morphological concepts and interpretation of

complex tissue patterns. Retrieval-augmented systems may further improve factual reliability by grounding generated responses in validated guidelines, institutional protocols or curated literature rather than relying entirely on parametric model memory (Xie *et al.*, 2023).

6. Spatial omics and the molecularization of tissue morphology

Conventional histopathology provides detailed spatial information but limited direct molecular resolution, whereas bulk molecular assays provide molecular information while averaging signals across tissue. Spatial transcriptomics and related spatial-omics methods address this separation by measuring molecular features while preserving their anatomical coordinates.

The clinical relevance of spatial information is particularly evident in cancer. Tumors are composed of heterogeneous cellular populations embedded within complex microenvironments containing immune cells, stromal cells, vascular structures and extracellular-matrix components. Spatial transcriptomics can identify molecularly distinct regions and characterize interactions between cellular populations that may be obscured in bulk sequencing (Anderson *et al.*, 2022).

Artificial intelligence provides an important analytical layer for these datasets. Spatial-omics experiments can generate thousands of molecular measurements across thousands of spatial locations, creating an analytical burden that exceeds conventional manual interpretation. Machine-learning methods can assist with spatial-domain identification, cell-type assignment, deconvolution, neighborhood analysis and integration with histological morphology (Rao *et al.*, 2021).

The convergence of spatial omics and digital pathology may ultimately create a new class of diagnostic information: molecular features that are interpreted according to their exact morphological context. Such integration could help characterize tumor invasion fronts, immune niches, therapy-resistant populations and biologically distinct microenvironments. However, cost, sample preparation, computational complexity and lack of standardized clinical workflows remain important obstacles to routine use (Pang *et al.*, 2024).

7. Liquid biopsy and longitudinal molecular pathology

Liquid biopsy extends pathology beyond the tissue specimen by enabling molecular interrogation of blood and other body fluids. Circulating tumor DNA, circulating tumor cells, extracellular vesicles and other analytes can provide information about tumor burden, genomic alterations and disease evolution. Unlike tissue biopsy, liquid biopsy can be repeated serially, making it particularly attractive for longitudinal monitoring (Ma *et al.*, 2024).

Circulating tumor DNA has attracted substantial attention for treatment monitoring and detection of molecular residual disease. Because tumor-derived DNA can decline or reappear in response to treatment, serial analysis may provide information before conventional imaging or clinical progression becomes evident (Ge *et al.*, 2024). The potential value of ctDNA is therefore complementary to tissue pathology rather than necessarily substitutive.

Analytical limitations remain important. Early-stage cancers may release very small quantities of tumor-derived DNA, and low-frequency variants may be difficult to distinguish from technical noise or clonal hematopoiesis. Preanalytical variables, assay sensitivity, sequencing depth and interpretation standards can therefore influence clinical performance (Ignatiadis *et al.*, 2021). AI and statistical learning may help identify patterns across serial measurements, but model outputs must remain anchored to analytically validated assays.

8. Artificial intelligence across laboratory medicine

AI adoption is not confined to anatomic pathology. Clinical laboratory medicine generates large longitudinal datasets that are well suited to machine-learning approaches. Applications include test-result interpretation, workflow optimization, quality control, demand forecasting, clinical decision support and detection of clinically meaningful patterns across multiple analytes (Baron, 2023).

Machine-learning approaches can complement conventional rule-based laboratory systems by modeling nonlinear relationships among variables. A laboratory result that appears only mildly abnormal in isolation

may become clinically important when interpreted alongside other analytes, previous results and patient characteristics. AI systems can potentially identify these multivariable patterns and prioritize results for clinical attention (Rabbani *et al.*, 2022).

In hematology, machine learning has been investigated for automated cell classification, abnormal-cell detection, leukemia screening and interpretation of high-dimensional analyzer outputs. These applications are attractive because hematology analyzers already generate multidimensional data, providing a structured environment for algorithm development and validation (Walter *et al.*, 2023).

Microbiology is similarly suitable for AI because modern diagnostic workflows combine microscopy, culture, antimicrobial susceptibility testing, MALDI-TOF mass spectrometry, molecular assays and genomic data. AI has been explored for pathogen identification, resistance prediction, classification of infection and laboratory surveillance. Integration with clinical metadata may further improve interpretation of complex infectious-disease patterns (Shelke *et al.*, 2023).

Recent reviews emphasize that AI implementation in laboratory medicine remains uneven. Barriers include data quality, interoperability, limited external validation, insufficient AI expertise and uncertainty about regulatory oversight. These challenges may be particularly pronounced in low- and middle-income settings where digital infrastructure and computational resources are limited (Oduoye *et al.*, 2024).

Table 2: Potential AI applications across pathology and laboratory medicine

Laboratory domain	AI-enabled application	Expected value	Major implementation concern
Anatomic pathology	Tumor detection, grading, biomarker quantification	Improved consistency and diagnostic efficiency	Domain shift and clinical validation
Digital pathology	Whole-slide triage and quantitative morphometry	Workload prioritization and reproducibility	Scanner/stain variability
Hematology	Cell classification and abnormality detection	Rapid screening and decision support	Rare-cell recognition and false negatives
Clinical biochemistry	Trend interpretation and anomaly detection	Contextual interpretation of longitudinal results	Data quality and clinical integration
Microbiology	Pathogen identification and resistance prediction	Faster and more integrated infection assessment	Changing epidemiology and assay variation
Molecular pathology	Variant prioritization and phenotype prediction	Improved interpretation of high-dimensional data	Interpretability and validation
Liquid biopsy	ctDNA pattern recognition	Longitudinal monitoring and residual-disease assessment	Low signal and clonal hematopoiesis
Spatial omics	Cellular/spatial domain identification	Molecularly resolved tissue characterization	Cost and standardization

9. Clinical translation and workflow integration

The value of AI in pathology and laboratory medicine should ultimately be measured by its effect on clinical workflow and patient outcomes rather than by algorithmic accuracy alone. A highly accurate model that is difficult to integrate into the laboratory information system, produces excessive alerts or increases review time may have limited practical value.

An effective implementation strategy should therefore define the clinical role of the model before deployment. AI may function as a screening tool, a second reader, a triage system, a quantitative measurement tool, a report-drafting assistant or a decision-support system. Each role requires a different validation framework and different safeguards.

Human oversight remains essential. AI outputs should be presented with appropriate uncertainty information and linked to the underlying evidence, such as the image regions or laboratory measurements that influenced the prediction. This approach may reduce automation bias and make disagreements between AI and professionals easier to investigate.

Workflow integration also requires continuous monitoring. Model performance can change when scanners are replaced, staining protocols are modified, patient populations shift or new disease patterns emerge. AI validation should therefore be viewed as a lifecycle process involving predeployment testing, prospective evaluation, postdeployment surveillance, version control and predefined procedures for model updating (Kelly *et al.*, 2019).

10. Bias, explainability, safety and governance

Bias is one of the most important threats to clinical AI. Models trained on limited institutional datasets may encode differences in patient demographics, disease prevalence, specimen preparation and imaging technology. External validation across multiple institutions is therefore essential to determine whether a model has learned generalizable pathology features or merely learned characteristics of the training environment (McGenity *et al.*, 2024).

Explainability is also challenging. Attention maps and heatmaps can identify image regions associated with predictions, but they do not necessarily demonstrate causal reasoning. Clinicians require information that is useful for verification, including the relevant tissue regions, supporting laboratory findings, confidence estimates and known limitations.

Generative AI introduces additional safety considerations because the output is not restricted to a predefined label. A model may generate a plausible differential diagnosis that contains unsupported assertions. For clinical use, systems should therefore be designed around constrained outputs, retrieval of authoritative information, explicit uncertainty and mandatory expert review.

Data governance is equally important. Pathology images and laboratory results are patient data, and foundation-model development may involve secondary use of large collections of clinical material. Institutions must address consent, de-identification, data ownership, access control, cybersecurity and governance of model outputs. Regulatory frameworks are also evolving, particularly for AI-enabled medical devices and laboratory-developed systems.

11. Future directions: Toward integrated diagnostic intelligence

The next stage of pathology and laboratory medicine is likely to involve integration rather than further development of isolated algorithms. A future diagnostic system may combine whole-slide morphology, immunohistochemistry, molecular profiles, spatial transcriptomics, ctDNA, routine laboratory tests and clinical information within a multimodal representation.

Table 3: Research priorities for clinical translation

Priority	Recommended direction
External validation	Use geographically and institutionally diverse cohorts rather than relying on internal test sets.
Prospective evaluation	Measure effect on diagnostic accuracy, turnaround time, workload and patient-relevant outcomes.
Dataset diversity	Include variation in demographics, scanners, staining, tissue processing and disease prevalence.
Uncertainty estimation	Require confidence, abstention or escalation mechanisms for difficult cases.
Human oversight	Design AI as a decision-support or copilot system with explicit professional responsibility.
Interoperability	Integrate AI with laboratory information systems, digital pathology platforms and clinical records.
Lifecycle monitoring	Track model performance after deployment and establish version-control and update procedures.
Data governance	Define consent, privacy, security, access, ownership and secondary-use policies.
Education	Train pathologists and laboratory professionals in AI limitations, validation and appropriate use.

Such integration could create a distinction between spatial and temporal diagnostic information. Tissue pathology provides a high-resolution spatial description of disease, whereas liquid biopsy can provide repeated measurements of molecular change over time. Routine laboratory tests provide physiological context, and clinical information provides the patient-level framework in which the results should be interpreted.

Foundation models may serve as the computational layer that connects these modalities. Rather than asking whether a particular slide contains cancer, a multimodal system could potentially summarize the evidence for diagnosis, identify discordant findings, suggest additional tests and present a structured evidence map for expert review. This represents a shift from image classification toward evidence integration.

Another emerging direction is workflow-aware or agentic AI. Such systems could retrieve relevant slides, laboratory results and previous reports, organize evidence, perform predefined analytical steps and prepare a draft interpretation for review. The development of such systems should remain tightly constrained by laboratory governance, auditability and human authorization rather than allowing unrestricted autonomous decision-making.

12. Conclusion

Pathology and laboratory medicine are moving from isolated diagnostic measurements toward an integrated computational ecosystem. Digital pathology established the infrastructure for large-scale quantitative analysis of tissue, while deep learning enabled automated recognition of morphological patterns. The emergence of foundation models now represents a further transition toward reusable, general-purpose pathology representations. Models such as UNI, CONCH, Virchow and Prov-GigaPath demonstrate how large-scale pretraining can support multiple downstream tasks, while multimodal systems such as PathChat show how pathology images can be connected with natural-language reasoning.

Spatial omics adds molecular information within its anatomical context, and liquid biopsy introduces longitudinal molecular monitoring. At the same time, AI is expanding throughout clinical laboratory medicine, including hematology, biochemistry, microbiology and laboratory decision support. The major opportunity is therefore not simply to automate individual diagnostic steps but to connect these information streams into a coherent patient-level representation.

Clinical translation will depend on rigorous external validation, representative datasets, interpretability, uncertainty estimation, data governance, regulatory oversight and sustained human supervision. AI should augment rather than replace the expertise of pathologists and laboratory professionals. The most clinically meaningful future is consequently one in which computational systems organize and integrate complex evidence while human experts remain responsible for final interpretation. The transition from whole-slide images to multimodal diagnostics may therefore redefine pathology and laboratory medicine as an integrated discipline of morphology, molecular biology, spatial information and computational reasoning.

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